SOUTHERN MEDICAL ASSOCIATION, Thirty-Ninth Annual Meeting, Cincinnati, November 12-15. The Campbell-Kenton County Medical Society of Kentucky is the host society. IT IS A KENTUCKY MEETING.

VOLUME 38 NOVEMBER 1945 NUMBER 11

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1945. Published monthly by the Southern Medical Association, Empire Building, Birmingham 3, Alabama. Annual subscription $4.00. Entered as Second-Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

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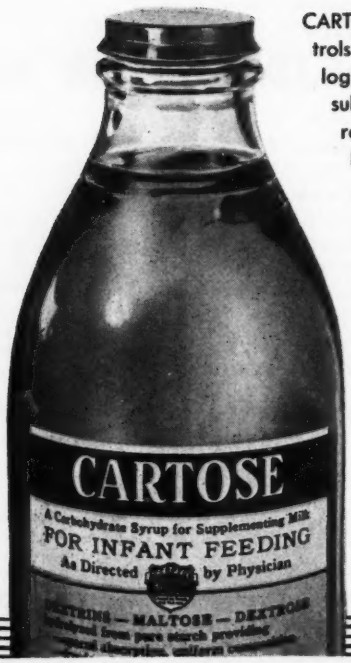

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3. Steck, I. E.: Clinical Experience in the Treatment of Arthritis with Massive Doses of Vitamin D, Peoria Medical News, *8*:2-7 (1937).
4. Steck, I. E.: Clinical Experience in the Treatment of Arthritis with Massive Doses of Vitamin D, Illinois Medical J. *71*:243-248 (1937).
5. Steck, I. E., Deutsch, H., Reed, C. I. and Struck, H. C.: Further Studies on Intoxication with Vitamin D, Annals of Internal Medicine, *10*:951-964 (1937).
6. Farley, R. T.: The Treatment of Arthritis with Massive Dosage Vitamin D, J. Amer. Inst. of Homeopathy, *31*:405-409 (July) 1938.
7. Reed, C. I., Struck, H. C. and Steck, I. E.: Vitamin D, Chemistry, Physiology, Pharmacology, Pathology, Experimental and Clinical Investigations, Pub. by University of Chicago Press (1939).
8. Farley, R. T.: Management of Arthritis, Ill. Med. J., *71*:74-77 (Jan.)1939.
9. Farley, R. T.: The Influence of Prolonged Administration of High Dosages of Vitamin D Upon the Serum Calcium of Adults, Journal-Lancet, *59*:401-404 (Sept.) 1939.
10. Snyder, R. G. and Squires, W. H.: A Preliminary Report on Activated Ergosterol, N. Y. State J. of Med., *40*:708 (May 1) 1940.
11. Farley, R. T., Spierling, H. F. and Kraines, S. H.: A Five-Year Study of Arthritic Patients, Indus. Med., *10*:341, 352 (Aug.) 1941.
12. Snyder, R. G. and Squires, W. H.: Follow-Up Study of Arthritic Patients Treated with Activated Vaporized Sterol, N. Y. State J. Med., *41*:2362 (Dec.)1941.
13. Steck, I. E.: Further Clinical Experience in the Treatment of Chronic Arthritis with Vitamin D, Ohio State Med. J., *38*:440 (May) 1942.
14. Snyder, R. G., Squires, W. H., Forster, J. W., Traeger, C. H. and Wagner, L. C.: Treatment of Two Hundred Cases of Chronic Arthritis with Electrically Activated Vaporized Sterol (Ertron), Indus. Med., *11*:295 (July) 1942.
15. Freyberg, R. H.: Treatment of Arthritis with Vitamin and Endocrine Preparations, J.A.M.A., *119*:1165 (Aug. 8) 1942.
16. Reynolds, C.: Comparative Therapeutic Value and Toxicity of Various Types of Vitamin D, Journal-Lancet, *62*:372-375 (Oct.) 1942.
17. Levinthal, D. H. and Logan, C. E.: The Orthopedic and Medical Management of Arthritis, Journal-Lancet, *63*:48 (Feb.) 1943.
18. Snyder, R. G., Squires, W. H. and Forster, J. W.: A Six-Year Study of Arthritis Therapy—With a Special Reference to the Pharmacology, Toxicology and Therapeutics, Indus. Med., *12*:291 (May) 1943.
19. Snyder, R. G., Squires, W. H., Forster, J. W., Rudd, E.: The Therapeutic Value of Electrically Activated Ergosterol when Administered Intramuscularly, Ind. Med.,*12*:663(Oct.)1943.
20. Reynolds, C. and Burns, E. L.: The Effect on the Rat of Prolonged Administration of Large Doses of Electrically Activated Ergosterol, Indus. Med., *12*:835 (Dec.) 1943.
21. Snyder, R. G., Squires, W. H., Forster, J. W. and Rudd, E.: Comparative Study of Ultraviolet Irradiated Ergosterol (Steenbock Process) and Electrically Activated Ergosterol (Whittier Process)—A Preliminary Report, Journal-Lancet, *64*:25 (Jan.) 1944.
22. Levinthal, D. H., Logan, C. E., Kohn, K. H. and Fishbein, W. I.: Practical Management of Arthritis—Medical and Orthopedic, Indus. Med. *13*:377 (May) 1944.
23. Traeger, C. H. Squires, W. H. and Rudd, E.: The Therapeutic Value of Electrically Activated Vaporized Ergosterol, Ind, Med., *14*:202-207 (Mar.) 1945.

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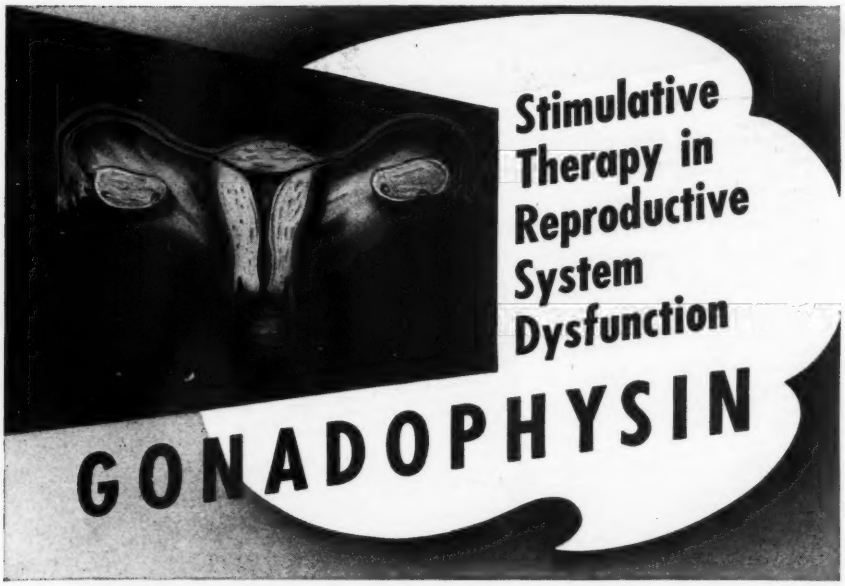

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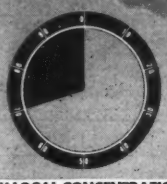

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Even though a child may be undernourished, his appetite often fails. To combat anorexia caused by a lack of important B vitamins, pediatricians increasingly prescribe 'Ryzamin-B' No. 2. Containing the natural B complex as a concentrate of oryza sativa (American rice) polishings, 'Ryzamin-B' No. 2 also supplies potent synthetic B factors. Children enjoy this rich, honey-like, tasty B complex preparation taken directly from the special measuring spoon, as a delicious spread when mixed with jam or peanut butter, or dissolved in milk, fruit juices, favorite beverages. The doctor often solves his commonest pediatric problem with 'Ryzamin-B' No. 2.

Tubes of 2 oz. and bottles of 8 oz. Each gram contains: Vitamin B_1 (Thiamine Hydrochloride) 1 mgm. (333 U.S.P Units); Vitamin B_2 (Riboflavin) 0.67 mgm; Nicotinamide 6.7 mgm. and other factors of the B complex. Gram measuring spoon with each packing.

'RYZAMIN-B' BRAND RICE POLISHINGS CONCENTRATE **No. 2**

WITH ADDED THIAMINE HYDROCHLORIDE, RIBOFLAVIN, NICOTINAMIDE

'Ryzamin-B' reg. trademark

BURROUGHS WELLCOME & CO. (U.S.A.) INC., 9 & 11 EAST 41ST ST., NEW YORK 17, N. Y.

Specific Action

TO PROMOTE FAT DIGESTION

When fat digestion is impaired due to deficient bile secretion, and when fatty foods prove intolerable in the absence of gallbladder involvement, Degalol—the original, chemically pure deoxycholic acid—offers noteworthy advantages.

A constituent of human bile, it is the fraction chiefly concerned with fat emulsification, promoting the digestion and absorption of ingested food fats and the utilization of the fat-soluble vitamins.

In the dosage required, Degalol exerts little or no choleretic influence. Thus it proves superior to ordinary bile salts which not only are less potent in their influence on fat emulsification, but—since they are required in higher dosage—produce side actions which are frequently undesirable. The powerful choleretic influence of the bile salts, for instance, is definitely to be avoided in catarrhal jaundice, though fat digestion and vitamin absorption are to be enhanced.

DOSAGE

One or two 1½ gr. tablets t. i. d. Supplied in boxes of 100 sanitaped 1½ gr. tablets. Available on prescription thru all pharmacies.

When fatty foods lead to postprandial distress and epigastric pain, Degalol frequently proves specific. In suspected or frank deficiency of fat-soluble vitamins D, E and K and carotene, the administration of Degalol together with the vitamins is indicated.

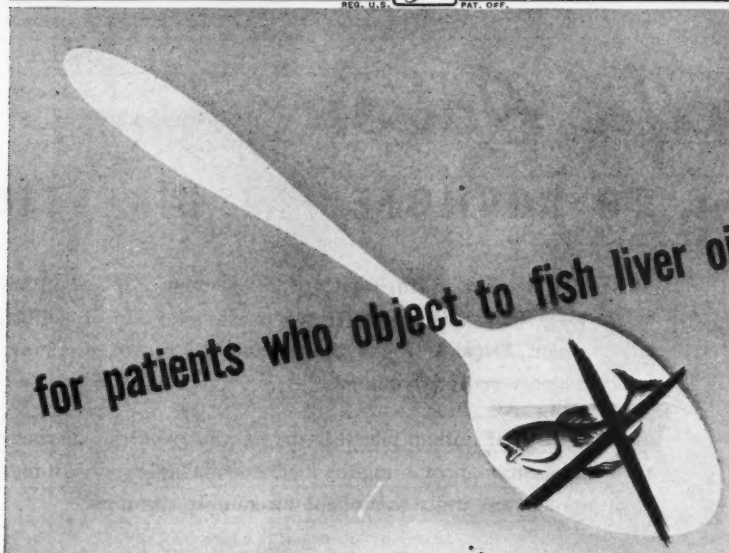
Degalol

REG U.S. PAT. OFF.

CHEMICALLY PURE DEOXYCHOLIC ACID

Riedel - de Haen, Inc. • New York 13, N. Y.

Wyeth
REG. U.S. PAT. OFF.



for patients who object to fish liver oil . . .

Provatol*

Liquid vitamins A and D in palatable form

PROVATOL is the only preparation available incorporating both vitamin A and D activity without resorting to fish liver oils.

VITAMIN A activity in Provatol is provided by carotene (provitamin A) extracted from vegetable sources and biologically stabilized with mixed tocopherols.

VITAMIN D activity is provided by irradiated ergosterol.

% MINIMUM DAILY REQUIREMENTS		
SUGGESTED DAILY DOSE	VITAMIN A ACTIVITY	VITAMIN D
Infants to 1 year—8 drops	135%	100%
Children 1 to 12 years—12 drops	100%	150%
Adults—16 drops	100%	200%

Supplied in 50 cc. bottles with dropper.

*REG. U. S. PAT. OFF.

Wyeth

S.M.A. DIVISION • WYETH INCORPORATED • PHILADELPHIA 3 • PA.

BALANCING THE CHILD'S NUTRITION

The diet of infants and young children naturally tends to be deficient in blood-building elements. This is due largely to the fact that milk, both human and cow's, is decidedly low in these factors. Armour *Liver, Iron and Red Bone Marrow* with Malt Extract is therefore a logical preparation for complementing the diet of these youngsters. It supplies the hemopoietic properties of Liver Extract, Iron, and Red Bone Marrow in combination with the caloric nutrient qualities of Malt Extract.

THE ARMOUR LABORATORIES

Chicago 9, Illinois

HEADQUARTERS FOR MEDICINALS OF ANIMAL ORIGIN

Available in 8 oz. bottles and special 2 oz. bottles with dropper (for infant feeding)

Each fluid ounce contains:

Liver Extract . . 10 cc.
Solution Liver Extract (Armour) derived from 75 grams of fresh liver.
Iron Ammonium Citrates 2.17 gms.
Red Bone Marrow . 10 cc.
The glycerinated extract from ½ ounce of the spongy red marrow structure of short ribs of young animals.
Malt Extract (Non-Diastatic) q. s.

Adult Dose 2 tsps. twice daily
Children (under 15 years) 1 tsp. twice daily
Infants . 1 to 10 drops daily (in milk or water)

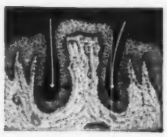
Liver, Iron and Red Bone Marrow (with malt extract)

Armour

in SORE THROAT

CĒPACOL
BRAND
ALKALINE GERMICIDAL SOLUTION

Cēpacol is rapidly effective against pathogenic bacteria associated with sore throat and, at the same time, acts as a mildly alkaline cleansing solution that allays irritation and soothes inflamed tissues.



PENETRATING—DETERGENT... Due to unusually low surface tension, recesses of the mucosa are reached by Cēpacol and cleansed by its foaming detergent action. In clinical use it is nontoxic, non-irritating, nonastringent, and does not interfere with healing.

PALATABLE... Cēpacol can be used as spray or gargle, full strength or diluted with an equal volume of water. Its delightful, refreshing flavor invites cooperation by the patient.

At prescription pharmacies in pints and gallons

Trademark "Cēpacol" Reg. U. S. Pat. Off.

MERRELL

THE WM. S. MERRELL COMPANY, CINCINNATI, U. S. A.

ILLUSTRATION BY ARTON OTTO FISCHER

"BY THE DEEP, SIX"

COMES THE CRY of the leadsman from his point on the bow, "By the deep, six"—safe water. Continuous soundings safeguard the course of a vessel in fog and in shallow channels . . . a final check against instruments and navigators' calculations.

For more than sixty-nine years Eli Lilly and Company has sought to safeguard the interests of the physician and to strengthen his position as a health factor by providing, in an ethical manner, medicinal agents of quality unexcelled. A "Lilly" specification on your prescription guarantees your patient the finest medication the markets of the world afford. Available through prescription stores everywhere.

Lilly

SMALLPOX *Vaccination*

FEW DISEASES have exercised a more profound influence on the lives of civilized people than smallpox. Once a dreaded scourge, the disease is now confined to sporadic outbreaks. Since immunity is developed in approximately eight to ten days after successful vaccination, it is possible to vaccinate contacts promptly after exposure and to prevent, or at least attenuate, the disease. Smallpox Vaccine, Lilly, is available in packages containing 1 immunization (V-1) and 5 immunizations (V-5), complete with rubber bulb for ejecting, and individually sealed, sterile needles for scarifying. Available through your regular source of medical supplies.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

No appreciable ciliary inhibition . . . Benzedrine Inhaler causes "no appreciable change in the amplitude or rapidity of the ciliary beat." Proetz A.W.: Arch. Otolaryng., 30:509.

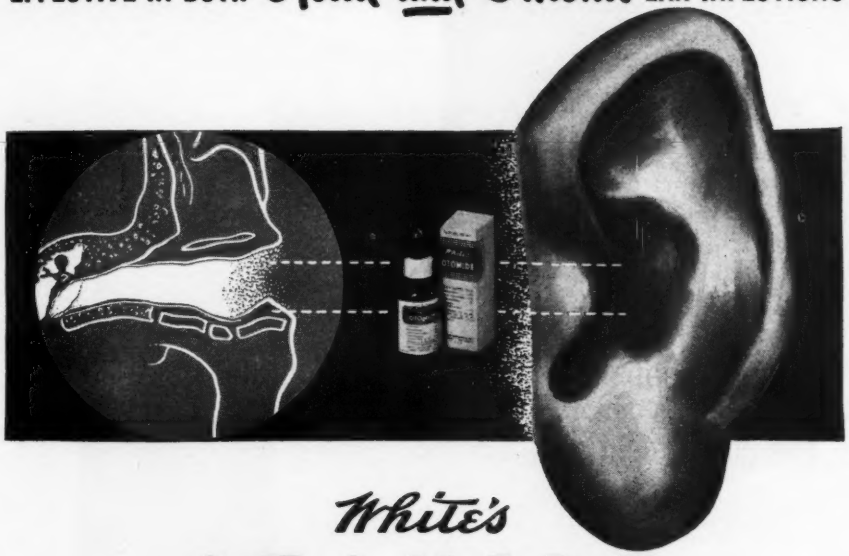
In addition, Benzedrine Inhaler, N. N. R., does not give rise to any significant degree of secondary turgescence, atony or bogginess, when used as directed.

The Inhaler is strikingly effective in reducing the congestion accompanying head colds, hay fever, and sinusitis. Each Benzedrine Inhaler is packed with racemic amphetamine, S. K. F., 200 mg.; menthol, 10 mg.; and aromatics. Smith, Kline & French Laboratories, Phila., Pa.

Benzedrine Inhaler

a better means of nasal medication

EFFECTIVE IN BOTH *Acute and Chronic* EAR INFECTIONS



White's

OTOMIDE

combines, in a vehicle of unusually high hygroscopic glycerin, sulfanilamide, urea and chlorobutanol. This *stable* solution offers numerous advantages in topical treatment of either *acute or chronic* middle and external ear infections caused by sulfonamide-susceptible organisms.

Summary of Advantages

Antibacterial Potency—even in the presence of pus.

Stability—a *stable* sulfonamide-urea solution.

Wide Field—effective in *BOTH* acute *AND* chronic middle and external ear infections.

Well Tolerated—physiologic pH—virtually obviating local irritation.

Analgesia—effective chlorobutanol analgesia *without* impaired sulfonamide activity.

Formula

Sulfanilamide	5%
Carbamide (urea)	10%
Chlorobutanol	3%
Glycerin (high sp. gr.)	q. s.

•

White's Otomide is available in dropper bottles of one-half fluid ounce (15 cc.)—*on prescription only.*

PHARMACEUTICAL White MANUFACTURERS

NEWARK 2, N. J.

synthetic
VITAMIN B COMPLEX
factors

for INTRAMUSCULAR • SUBCUTANEOUS • INTRAVENOUS *administration*

Stable

BETASYNPLEX "NIPHANOID" contains the five important synthetic components of vitamin B complex in dry and stable form for parenteral use.

Large doses in small volume

Each ampul contains:

***Thiamine* hydrochloride (vitamin B_1)**	***10 mg.***
***Riboflavin* (vitamin B_2, as soluble salt of riboflavin sodium—sodium tetraborate)**	***5 mg.***
***Pyridoxine* hydrochloride (vitamin B_6)**	***5 mg.***
Calcium pantothenate	***5 mg.***
***Niacinamide* (nicotinic acid amide)**	***50 mg.***

Effective

The addition of only 2 cc. of distilled water yields almost instantly a fresh solution of full potency. The therapeutic efficiency of synthetic vitamins has been firmly established by clinical experience. BETASYNPLEX "NIPHANOID" is of particular value for patients who vomit or fail to absorb oral doses because of other gastro-intestinal disturbances.

Supplied in boxes of 3, 10 and 50 ampuls.

FOR ORAL USE: BETASYNPLEX TABLETS AND ELIXIR WITH OR WITHOUT IRON

BETASYNPLEX *"Niphanoid"*

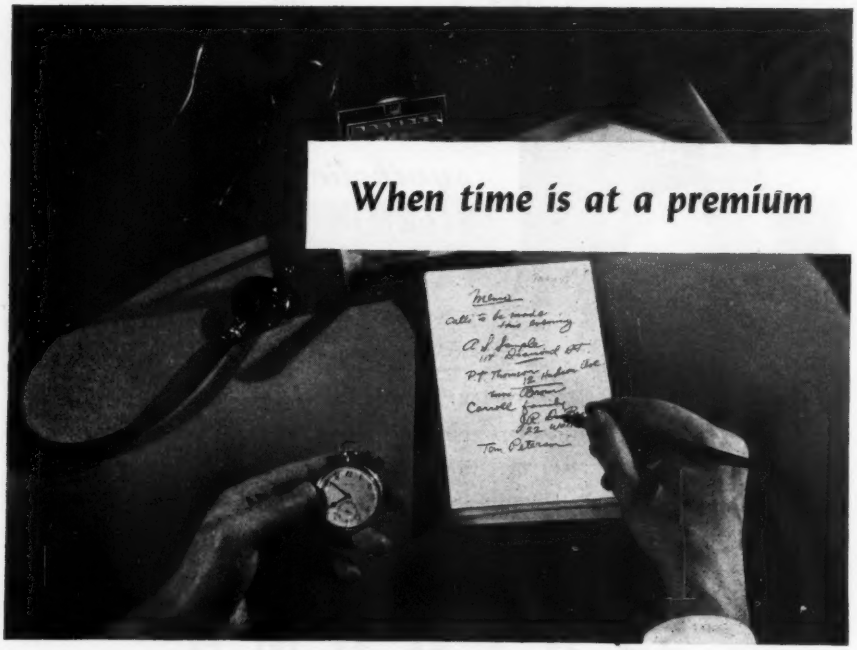
TRADEMARK REG. U.S. PAT. OFF. & CANADA

WRITE FOR DETAILED LITERATURE

Winthrop Chemical Company, Inc.

PHARMACEUTICALS OF MERIT FOR THE PHYSICIAN

NEW YORK 13, N. Y. • WINDSOR, ONT.



PYRIDIUM

(REG. U. S. PAT. OFF.)

affords several distinct advantages

EASE AND CONVENIENCE OF ADMINISTRATION

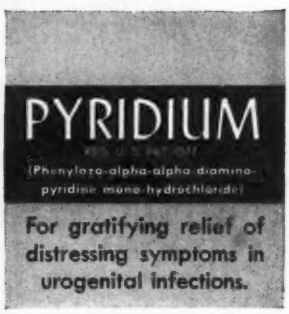
Pyridium is convenient to administer. No laboratory control, accessory medication, or other special measures are necessary for effective Pyridium therapy.

LACK OF TOXICITY

Therapeutic doses of Pyridium may be administered with complete safety throughout the course of cystitis, pyelonephritis, prostatitis, and urethritis.

RAPID RESPONSE

Prompt, *gratifying* relief of distressing urinary symptoms is the characteristic response to Pyridium therapy.


PYRIDIUM
(Phenylazo-alpha-alpha diamino-pyridine mono-hydrochloride)
For gratifying relief of distressing symptoms in urogenital infections.

MERCK & CO., Inc. *Manufacturing Chemists* RAHWAY, N. J.

Announcing...

PENICILLIN OINTMENT SCHENLEY

It is possible by topical application to reach local levels of penicillin activity far in excess of the highest ranges maintained by intravenous and intramuscular administration.

Penicillin Ointment Schenley is indicated in the treatment of superficial infections of the skin caused by penicillin-sensitive organisms. In deep-seated pyogenic infections with penicillin-sensitive organisms, the ointment may be used as an adjunct to systemic penicillin therapy and other measures.

When you specify Penicillin Ointment Schenley, you are assured of the highest standard of excellence, because Schenley Laboratories maintains the same rigid program of control for this ointment as it has always maintained for Penicillin Schenley.

SCHENLEY LABORATORIES, INC.
Executive Offices: 350 Fifth Avenue, New York City

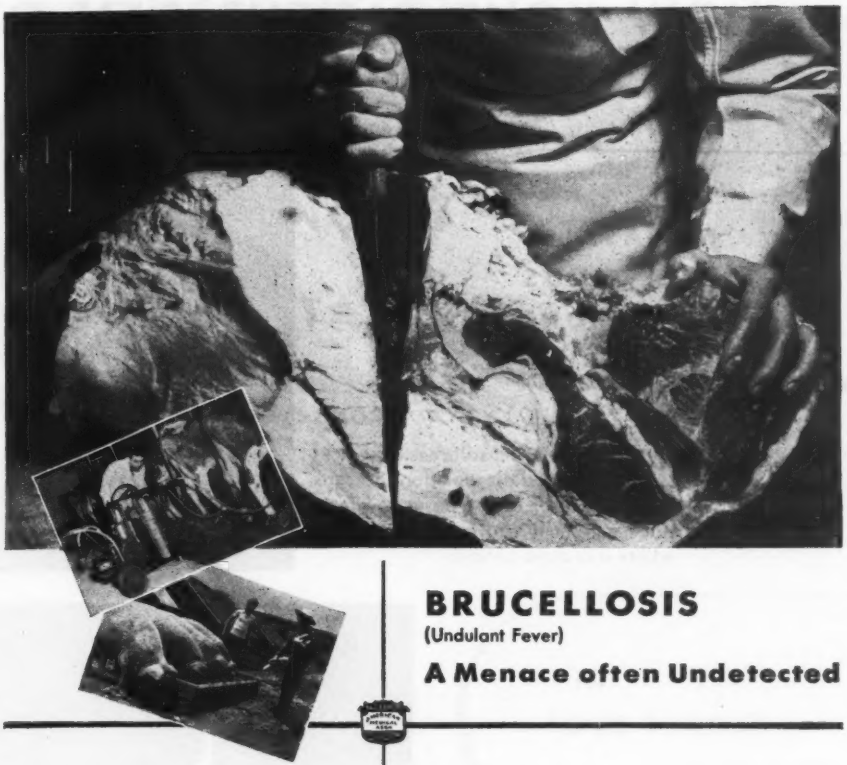
The mythical Achilles had but one vulnerable spot, but the pregnant woman is systemically vulnerable—vulnerable to deficiencies in calcium, phosphorus and vitamin D. When pregnant women neglect or refuse a balanced diet, their babies, as well as they, are the losers.

Protection in regard to these elements can be simply conferred when SQUIBB Dicalcium Phosphate with Viosterol (2 capsules, 3 times daily) is added to the average diet.

Dicalcium Phosphate Compound

SQUIBB

MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858



BRUCELLOSIS

(Undulant Fever)

A Menace often Undetected

Undulant Fever Vaccine
(Melitensis) (Bio. No. 60)
Brucella melitensis . . . 2000 million per cc.

Undulant Fever Vaccine
(Abortus and Suis) (Bio. No. 62)
Brucella abortus . . . 1000 million per cc.
Brucella suis . . . 1000 million per cc.

Both available in 6 cc. and 20 cc. vials. Selection of type of vaccine depends upon the history of the case.
Full literature on request.

"FIFTEEN years ago observed as a curiosity," Brucellosis is estimated as existing in "*ten to fifteen per cent of the American population*" . . . but unfortunately only "*one per cent or less* of infected cases reach detection and treatment."*

Whatever the source of infection—be it bovine, porcine, or other animal origin—Pitman-Moore Biological Laboratories offer a vaccine to meet your therapeutic requirements.

*Staub, R. R.: Brucellosis, An Unrecognized Menace, Northwest Med., 43:274-479 (Oct.), 1944.

PITMAN-MOORE COMPANY
PHARMACEUTICAL AND BIOLOGICAL CHEMISTS
Division of Allied Laboratories, Inc. · Indianapolis 6, Indiana

HOW YOUR PATIENT CAN OBTAIN

IN NASAL AND SINUS INFECTIONS

WRONG

When the patient instills nasal medication in an upright position, it runs along the floor of the nose, and does not reach many of the engorged areas where it is most needed.

RIGHT

But when the patient assumes a dependent, head-low posture, Paredrine-Sulfathiazole Suspension spreads rapidly and evenly, effecting prompt vasoconstriction and prolonged bacteriostasis *precisely* where they are needed most.

PAREDRINE-SULFATHIAZOLE

VASOCONSTRICTION IN MINUTES BACTERIOSTASIS FOR HOURS

IN SORE THROAT

So that Paredrine-Sulfathiazole Suspension will remain on infected areas hour after hour, and thus maintain its maximum bacteriostatic action, the sore throat patient should be advised: (1) to instill the Suspension intranasally *after* eating and just *before* retiring; (2) to refrain from drinking fluids as long as possible after each instillation; and (3) to reduce nose-blowing and throat-clearing to a minimum. Smith, Kline & French Laboratories, Philadelphia, Pa.

AZOLE SUSPENSION

Unconditional Surrender *Every Time!*

There is no stalling or quibbling on the part of small children when a palatable, liquid preparation such as Vi-Daylin is given. Most children have difficulty in swallowing tablets or capsules while many others refuse to accept the older types of heavy emulsions and the less pleasant-tasting malt products. Vi-Daylin, therefore, is especially adapted to administering the daily vitamin supplements to infants and children. Vi-Daylin is a stable, homogenized mixture of vitamins A and D, thiamine hydrochloride, riboflavin, ascorbic acid, and nicotinamide. It contains only traces of alcohol (not more than 0.5 percent) and one teaspoonful, 5 cc., supplies at least *twice* the minimum daily requirements for infants of vitamins A and D and riboflavin, at least *three times* that of vitamin B_1, *four* times that of vitamin C, and more than the recommended daily allowance of nicotinamide. Vi-Daylin mixes readily with cereal, milk or juices but both children and adults enjoy its citrus-fruit flavor when it is given by spoon as it comes from the bottle. Vi-Daylin is carefully standardized for each of the contained vitamins. It is available through prescription pharmacies everywhere in 90-cc. bottles. ABBOTT LABORATORIES, North Chicago, Illinois.

Vi-Daylin
TRADE MARK

(Homogenized mixture of vitamins A, D, B_1, B_2, C and Nicotinamide, Abbott)

WHEN THE NATURAL
PRODUCTION OF
MALE SEX
HORMONE
DIMINISHES with declining gonadal function, replacement therapy with ORETON will offset the androgenic inadequacy.

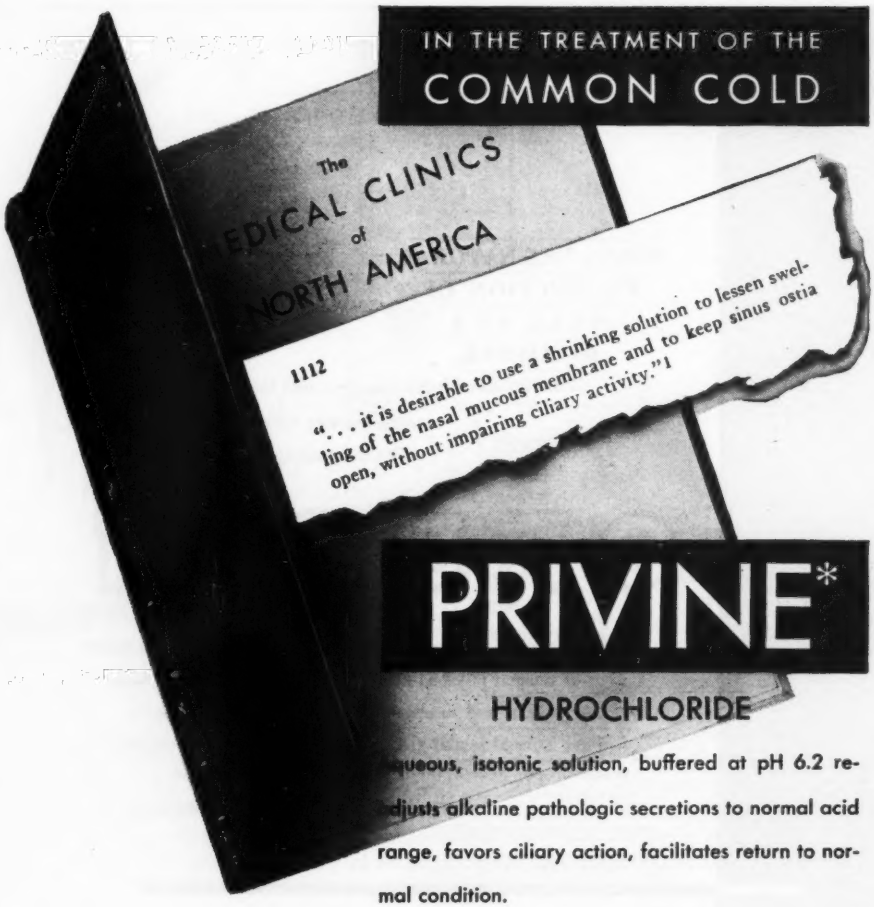
ORETON

supplies the needed male sex hormone for maintenance of normal physical and emotional balance in the male climacteric and in other androgen deficiency states.
When normal sexual growth is retarded in the formative years, proper development of the male genitalia and secondary sex characteristics may be achieved with ORETON.

PACKAGING: ORETON (testosterone propionate in oil) for intramuscular injection. Ampules of 1 cc. containing 5, 10, 25 mg. Boxes of 3, 6 and 50 ampules.

TRADE-MARK ORETON—REG. U. S. PAT. OFF

Schering CORPORATION • BLOOMFIELD, N. J.


IN THE TREATMENT OF THE
COMMON COLD
The
EDICAL CLINICS
of
NORTH AMERICA
1112
". . . it is desirable to use a shrinking solution to lessen swelling of the nasal mucous membrane and to keep sinus ostia open, without impairing ciliary activity."1
PRIVINE*
HYDROCHLORIDE

queous, isotonic solution, buffered at pH 6.2 readjusts alkaline pathologic secretions to normal acid range, favors ciliary action, facilitates return to normal condition.

Privine (Naphazoline) provides prolonged relief of congestion in acute rhinitis . . . not followed by secondary vasodilatation. 0.1% for adults; 0.05% for children; bottles of 1 oz.

1. Medical Clinics of North America, 1108, Sept. 1944.

*Trade Mark Reg. U. S. Pat. Off.

a Ciba Product

CIBA PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY
IN CANADA, CIBA COMPANY LIMITED, MONTREAL

Sharp & Dohme

'PROTHRICIN'

Antibiotic Nasal Decongestant containing Tyrothricin and 'Propadrine' Hydrochloride

An antibiotic and vasoconstricting agent for prompt relief of nasal congestion accompanying bacterial infections.

'PROTHRICIN' decongestant provides a double control for the symptomatic treatment of nasal congestion accompanying the common cold, allergic rhinitis, acute catarrhal rhinitis, acute rhinosinusitis and acute ethmoiditis.

An isotonic solution with a *pH of 5.5 to 6.5*, 'PROTHRICIN' decongestant is ideally suited for topical application to the mucous membrane of the nose and accessory sinuses.

The active ingredients of this preparation are:

Tyrothricin (antibiotic) . . 0.02%
(200 micrograms per cc.)

'Propadrine' Phenylpropanolamine Hydrochloride
(vasoconstrictor) 1.50%

Applied by means of tampons, irrigation, drops or spray. Supplied in 1-ounce bottles with dropper assembly. Sharp & Dohme, Phila. 1, Pa.

PROGYNON-DH

Alpha-estradiol, the true follicular hormone in tablets

PROGYNON-B

Benzoate of the natural estrogenic hormone for injection

PROGYNON-B and PROGYNON-DH are forms of the true estrogenic hormone, unsurpassed for potency and safety. These are preparations of choice when high standards of medical therapy call for the "best". Follicular hormone deficiencies can be controlled most effectively with full therapeutic safety when Schering's PROGYNON preparations are used for injection (in ampules), for oral administration (tablets and solution) and for inunction (ointment).

TRADE-MARKS PROGYNON-B AND PROGYNON-DH—REG. U. S. PAT. OFF.

Schering CORPORATION • BLOOMFIELD, N. J.

✓ *"Premarin" is an orally active estrogen of proved clinical effectiveness. The rapidly expanding bibliography provides ample evidence of its value in clinical practice.*

✓ *While "Premarin" is one of the most highly potent estrogens available, it is exceptionally well tolerated, and untoward effects are rarely noted.*

✓ *"Premarin" is derived exclusively from natural sources, and is earning increasing recognition for its desirable property of imparting a feeling of well-being.*

✓ *"Premarin" provides a convenient form of therapy for both physician and patient. It is available in tablet form in two potencies: No. 866 (yellow tablet) for the more severe deficiency, and No. 867, Half-Strength (red tablet), where a milder estrogen is required.*

Standardized by colorimetric and biological methods and supplied with the approval of the Research Institute of Endocrinology, McGill University.

"Premarin" TABLETS

ACCEPTED AMERICAN MEDICAL ASSN.

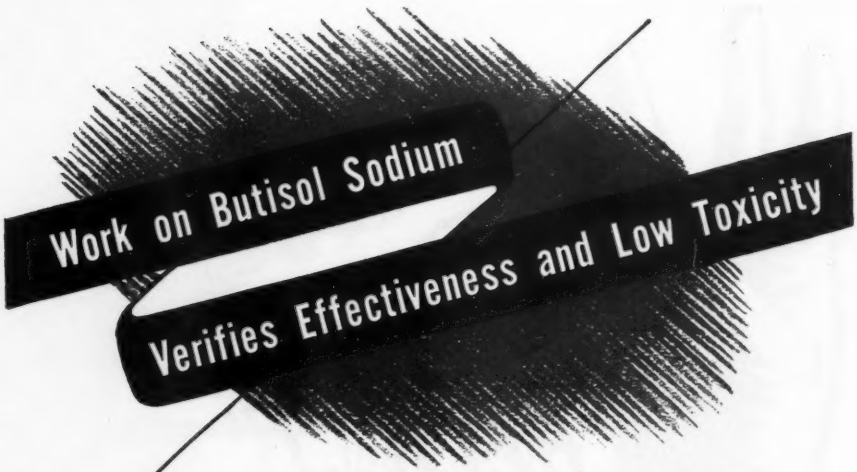
CONJUGATED ESTROGENS (equine)

No. 866, in bottles of 20, 100 and 1000 tablets; No. 867 (Half-Strength) in bottles of 100 and [illegible] tablets

AYERST, McKENNA & HARRISON LIMITED . . . Pioneers of Oral Estrogens

Rouses Point, N. Y. New York 16, N. Y. (U. S. Executive Offices) Montreal, Canada

Ayerst



Described as an "intermediate" between the fast-acting sedatives such as pentobarbital and the long-acting drugs such as phenobarbital and barbital,

BUTISOL SODIUM

(Sodium salt of 5 ethyl-5-secondary butyl barbituric acid "McNeil")

was studied by Gruber et al* and found to have unique pharmacologic properties:

- **duration of action "intermediate" between short-acting and long-acting barbiturates**
- **destruction in the body and not dependent upon renal excretion**
- **low toxicity in effective dosage**
- **therapeutic coefficient on rabbits found to be better than phenobarbital sodium and approximately equal to pentobarbital sodium**
- **little excitement during induction**
- **minimum barbiturate "hangover"**

Butisol Sodium is indicated in insomnia, neuroses, relief of preoperative apprehension, obstetrical hypnosis, daytime sedation and menopausal hysteria.

Supplied in capsules containing 1½ grs.; bottles of 100, 500 and 1000. Elixir Butisol Sodium, 3 gr. per fl. oz. is supplied in bottles of one pint. Clinical trial supply mailed to physicians on request. Caution: Use only as directed.

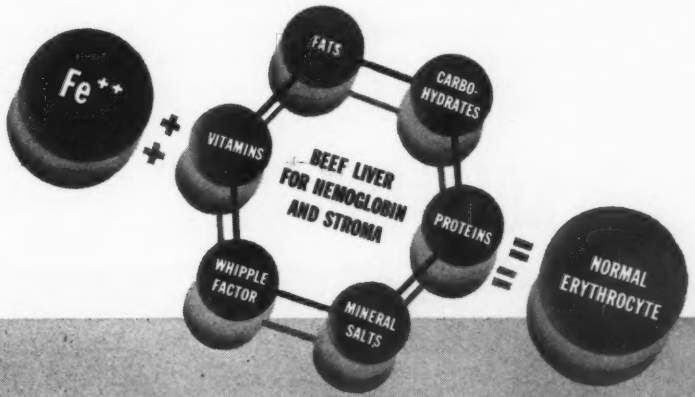
*Gruber, C. M., Ellis, F. W. and Freedman, G. J. Pharmacol. & Exper. Therap. *81*:254 (July) 1944

McNeil Laboratories
INCORPORATED
PHILADELPHIA • PENNSYLVANIA

Wyeth
REG. U.S. PAT. OFF.

CHRONIC ANEMIA

MAY REQUIRE MORE THAN IRON FOR RECOVERY



Accent on Liver

BĒPRON* supplies whole, unfractionated beef liver with saccharated ferrous iron. Liquid in half-pints, pints and gallons. Capsules in bottles of 100 and 500.

Accent on Iron

HEMATINIC PLASTULES* with Liver Concentrate supply dried ferrous sulfate with liver and yeast concentrates. Bottles of 50, 100 and 1000.

HEMATINIC PLASTULES Plain are effective in uncomplicated iron deficiency anemia. Each Plastule contains 5 grains dried ferrous sulfate with yeast concentrate. Bottles of 50, 100 and 1000.

*REG. U. S. PAT. OFF.

Wyeth

WYETH INCORPORATED • PHILADELPHIA 3 • PA.

effectiveness established: results striking!

THESE TWO BRIEF PHRASES graphically describe 'SULFASUXIDINE' *succinylsulfathiazole*—the sulfonamide that has been accepted widely as a drug of choice for bacteriostasis in intestinal surgery.

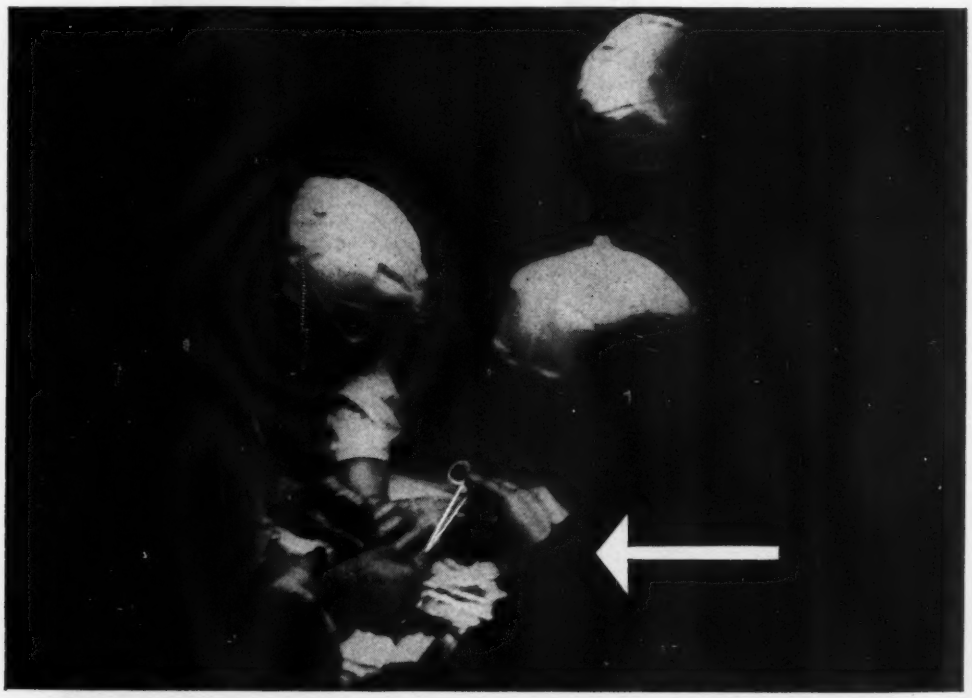
Because of the drug's exceptional effectiveness as an enteric bacteriostat, the physician has a valuable therapeutic weapon with which to combat certain intestinal infections.

A recent report states: "We have been using the drug routinely (preoperatively) for two years in all patients who are to have intestinal resections. The reduction in the incidence of peritonitis, a smoother convalescence and the reduction in the overall mortality have been so striking that there can be little doubt that sulfasuxidine played its part."[1]

'SULFASUXIDINE' *succinylsulfathiazole* has demonstrated its therapeutic value also in the treatment of acute or chronic bacillary dysentery, as well as the carrier state, and in ulcerative colitis.

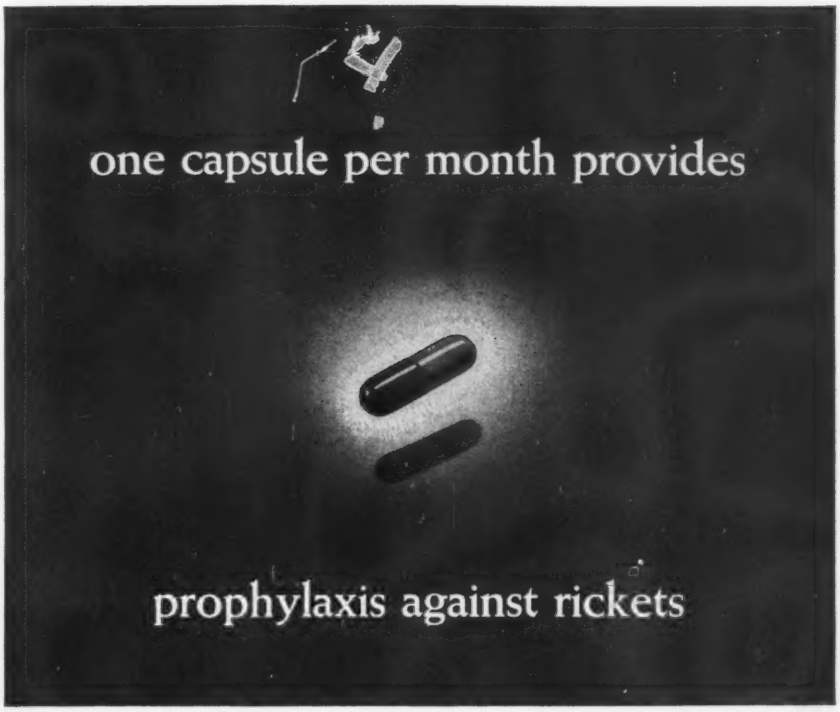
Supplied in 0.5 Gm. tablets in bottles of 100, 500 and 1,000, as well as in powder form (for oral administration) in ¼ and 1-pound bottles. Sharp & Dohme, Philadelphia 1, Pa.

Sharp & Dohme 'SULFASUXIDINE' *Succinylsulfathiazole*



This product is now officially available on the supply table of both the Army and Navy.

1. Gastroenterology 4:20-22, Jan. 1945.



No longer is the administration of antirachitic medication a problem for busy mothers. The convenience and economy of once-a-month dosage as provided in

Infron
Pediatric

are obvious. Infron Pediatric taken once a month, is adequate prophylaxis against rickets and other calcium deficiencies.

Infron Pediatric is readily miscible in the infant's feeding formula, milk, fruit juices, or water, and can also be spread on cereal. Each capsule of Infron Pediatric contains 100,000 U.S.P. Units of Vitamin D—Whittier Process—especially prepared for pediatric use.

Supplied in packages of 6 capsules—sufficient dosage for 6 months. Available at prescription pharmacies.

The effectiveness and safety of Infron Pediatric are confirmed in the published work of Wolf, Rambar, Hardy and Fishbein.

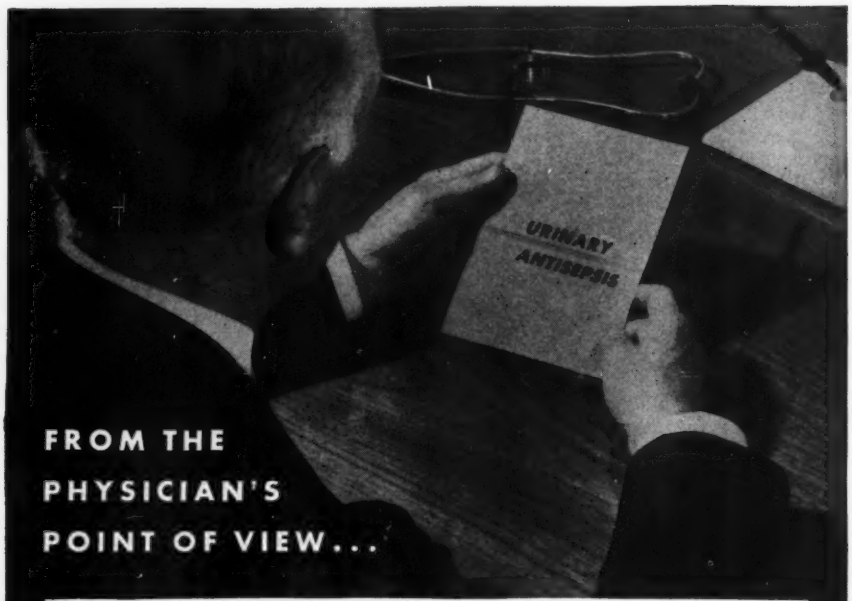
ETHICALLY PROMOTED

REFERENCES

Rambar, A. C., Hardy, L. M. and Fishbein, W. I.: J. Ped. 23:31-38 (July) 1943
Wolf, I. J.: J. Ped., 22:707-718 (June) 1943
Wolf, I. J.: J. Ped., 22:396-417 (April) 1943
Wolf, I. J.: J. Med. Soc. New Jersey, 38:436 (Sept.) 1941

Infron is the registered trademark of Nutrition Research Laboratories.

NUTRITION RESEARCH LABORATORIES · CHICAGO



FROM THE
PHYSICIAN'S
POINT OF VIEW...

These distinctive attributes suggest

MANDELAMINE

Reg. U. S. Pat. Off.
(Methenamine Mandelate)

- Lack of Toxicity
- Convenience of Therapy
- Prompt, Effective Action
- Wide Range of Therapeutic Activity

Mandelamine is supplied in enteric coated tablets of 0.25 Gm. (3¾ grains) each, in packages of 120 tablets sanitaped, and in bottles of 500 and 1000.

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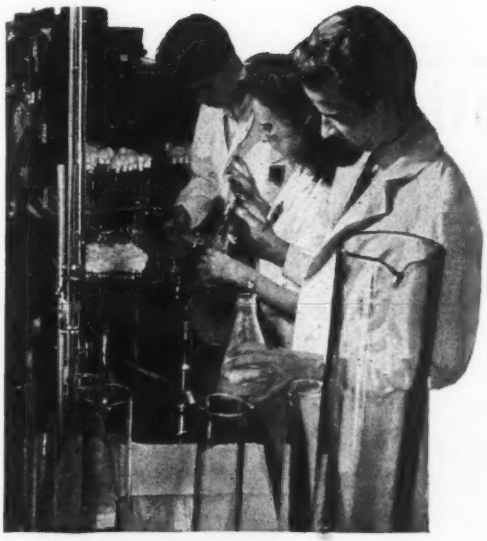
21 Gray Oaks Ave.
Yonkers 2, New York
Please send me literature, and a physician's sample of Mandelamine.

Name.....M.D.
Street.....
City.....State.....

NEPERA CHEMICAL CO. INC.

Manufacturing Chemists Yonkers 2, New York



MERCK VITAMINS

Thiamine Hydrochloride U.S.P.
(Vitamin B_1 Hydrochloride)

Riboflavin U.S.P.
(Vitamin B_2)

Niacin
(Nicotinic Acid U.S.P.)

Niacinamide
(Nicotinamide U.S.P.)

Pyridoxine Hydrochloride
(Vitamin B_6 Hydrochloride)

Calcium Pantothenate Dextrorotatory

Ascorbic Acid U.S.P.
(Vitamin C)

Vitamin K_1
(2-Methyl-3-Phytyl-1,4-Naphthoquinone)

Menadione U.S.P.
(2-Methyl-1,4-Naphthoquinone)
(Vitamin K Active)

Alpha-Tocopherol
(Vitamin E)

Alpha-Tocopherol Acetate

Biotin

PURE VITAMINS

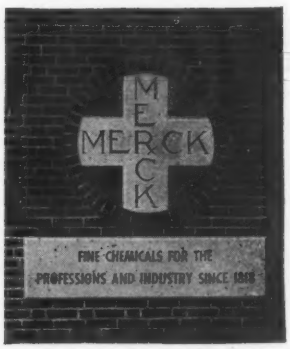
—products of Merck Research

Merck research has been directly responsible for many important contributions to the synthesis, development, and large-scale production of individual vitamin factors in pure form.

In a number of instances, the pure vitamins may be considered to be products of Merck research. Several were originally synthesized in the Merck Research Laboratories, and others have been synthesized by Merck chemists and collaborators in associated laboratories.

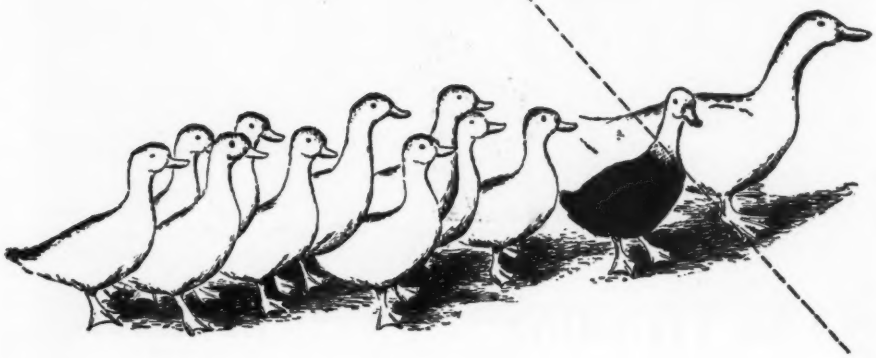
Because most of the known vitamins have now been made available in pure form, effective therapy of specific vitamin deficiencies can be conducted on a rational and controlled basis, under the direction of the physician.

Merck & Co., Inc. now manufactures all the vitamins commercially available in pure form, with the exception of vitamins A and D.



MERCK & CO., Inc. *Manufacturing Chemists* **RAHWAY, N. J.**

for both **exception** *and the rule*



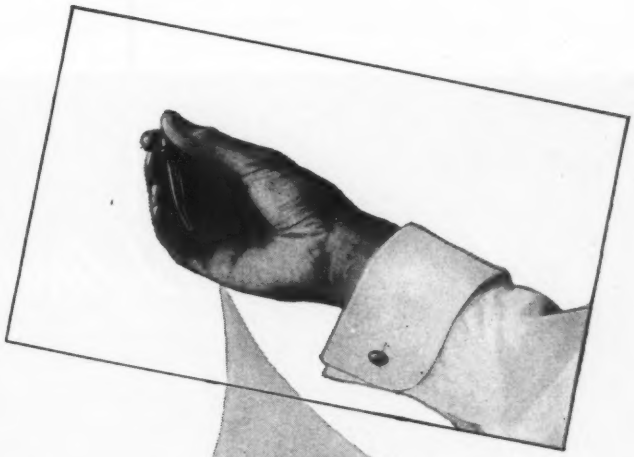
While functional constipation is usually founded on long-term neglect, exceptional circumstances often bring transient distress to otherwise careful individuals. Dietary indiscretion, a sudden change in environment, travel and other modifications in the daily routine are frequent precipitating factors.
Whether constipation be the exception or the rule, the return to normal bowel function is favored by the gentle moderating action of

'agarol'* *Emulsion*

*Trademark Reg. U. S. Pat. Off.

Replacing deficient bulk and lubricating factors while providing the minimal threshold stimulus for comfortable evacuation, 'AGAROL' Emulsion offers a simple, safe and reliable means of treatment.
Supplied in bottles of 6, 10 and 16 fluidounces.

WILLIAM R. WARNER & CO., INC., 113 West 18th Street, New York 11, N. Y.



the UPPER HAND in COLDS

When nostrils are blocked during coryza, allergic rhinitis, sinusitis, or any of the many other conditions which produce turbinate edema, 'Vaporole' brand Ephedrine Isotonic Solution (aqueous) brings quick relief. Nasal passages clear promptly without mucosal irritation, ciliary action continues unimpaired, vasoconstriction is immediate and prolonged. Pleasantly aromatic, non-stinging, in a non-oily vehicle, 'Vaporole' Ephedrine Isotonic Solution (aqueous) is especially liked by children.

'VAPOROLE' EPHEDRINE ISOTONIC SOLUTION (Aqueous)
containing 1 percent ephedrine in an isotonic solution of sodium, potassium and calcium chlorides and dextrose (modified Locke's solution) . . . Bottles of 1 fluidounce and 1 pint.

'VAPOROLE' Reg. Trademark.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., 9 & 11 EAST 41ST STREET, NEW YORK 17, N.Y.

A New and Definite Advance

IN THE TREATMENT OF

IRON-DEFICIENCY ANEMIAS

White's

MOL-IRON

TABLETS

A *specially processed*, co-precipitated complex of molybdenum oxide (3 mg.) and ferrous sulfate (195 mg.), White's Mol-Iron is a new, highly effective, hemopoietic agent that has unique therapeutic advantages in iron-deficiency anemias.

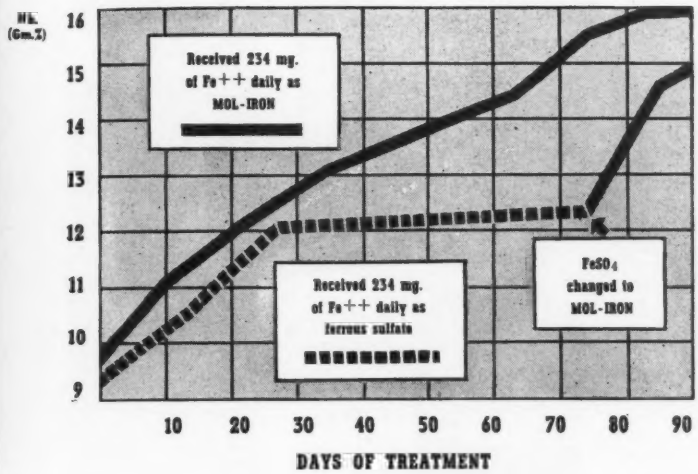
Available clinical evidence indicates that Mol-Iron effects approximately:

1. **100% GREATER THERAPEUTIC UTILIZATION OF IRON,** and

2. **100% MORE RAPID REGENERATION** of hemoglobin than does ferrous sulfate, with

3. **NOTABLE ABSENCE OF GASTRO-INTESTINAL REACTIONS**—even among patients exhibiting such untoward symptoms during administration of other commonly used iron preparations.

TYPICAL HEMOGLOBIN RESPONSE TO MOL-IRON AND TO FERROUS SULFATE IN PREGNANT WOMEN WITH IRON-DEFICIENCY ANEMIAS



The therapeutically superior effect of Mol-Iron in human beings is well demonstrated in the accompanying graph which illustrates the rate of hemoglobin regeneration in females during the last half of pregnancy and having approximately the same degree of iron-deficiency anemia. Results in this series of cases are typical of those observed in an evaluation* of Mol-Iron in a series of pregnant women with hypochromic anemia.

May we suggest that you make a comparable evaluation of Mol-Iron with your presently preferred therapeutic iron compound.

DOSAGE: One to two tablets three times daily after meals.

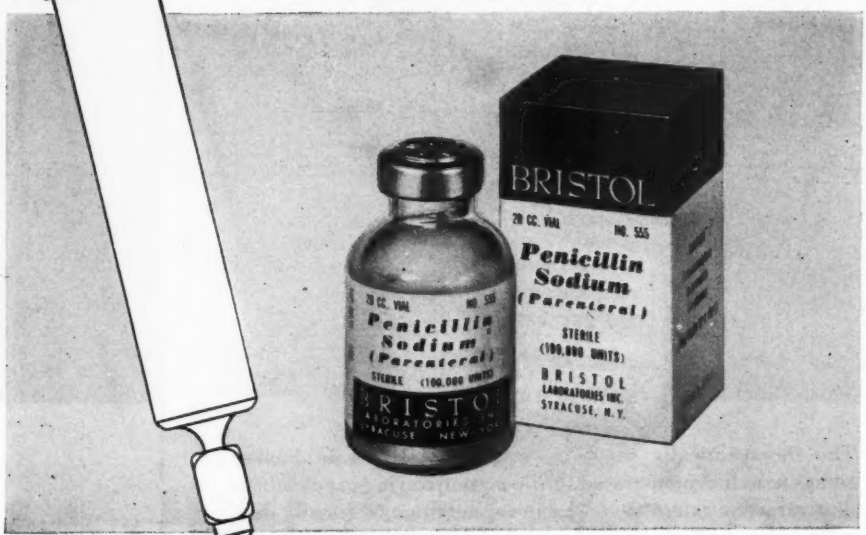
SUPPLIED: in bottles of 100.

*Neary, E. R., Preliminary Evaluation of Molybdenum-Iron Complex in Hypochromic Anemias of Pregnancy, to be published.

PHARMACEUTICAL White LABORATORIES, INC. NEWARK 2, N. J. MANUFACTURERS

COMPLICATIONS FROM PENICILLIN

The use of purer penicillin has markedly reduced such complications as phlebitis, pain at the site of injection, pyrexia, vascular and sympathetic disturbances, as well as muscular cramps.*



When you employ Bristol Penicillin in your practice you will find it:

1. **Uniformly high in potency per milligram and**
2. **Markedly light in color.**

Order Bristol Penicillin through your physician's or hospital supply house.

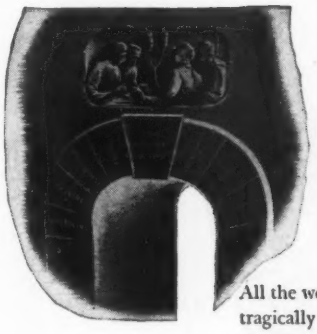
BRISTOL PENICILLIN

*Keys, J.E.L.: Penicillin in Ophthalmology. J.A.M.A. 126: 610 (Nov. 4) 1944.

BRISTOL LABORATORIES INCORPORATED

Formerly Cheplin Laboratories Inc.

SYRACUSE 1, NEW YORK



Vital Support
in Modern Surgery

All the wealth of modern surgical skill and knowledge may be tragically unavailing if the patient is physically unfit for operation. In poorly nourished patients, preoperative correction of hypoproteinemia lessens surgical risk . . . hastens healing. Parenamine—clinically proved parenteral substitute for dietary protein—restores and maintains positive nitrogen balance . . . corrects hypoproteinemia . . . stimulates regeneration of tissue and serum proteins.

Parenamine

AMINO ACIDS STEARNS PARENTERAL

For protein deficiency

PARENAMINE is a sterile 15 per cent solution of all the amino acids known to be essential for humans, derived by acid hydrolysis from casein and fortified with pure *dl*-tryptophane. Sterility, freedom from pyrogens, and standardization of each batch are meticulously checked by laboratory procedures, animal testing, and injection of full therapeutic doses clinically.

INDICATED in protein deficiencies and conditions of restricted intake, faulty absorption, increased need, or excessive loss of proteins. Particularly useful in preoperative and postoperative management, nephrotic-toxemia of pregnancy, extensive burns, delayed healing, gastrointestinal disorders, cirrhosis, nephrosis, fevers, and other hypermetabolic states.

ADMINISTRATION may be intravenous, intrasternal or subcutaneous. Dosage may be estimated at 1 Gm. amino acids per kilogram of body weight per day, plus sufficient excess to correct the existing deficiency.

SUPPLIED as 15 per cent sterile solution in 100 cc. rubber-capped bottles.

Complete clinical information will be gladly sent on request.

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A Reputation earned over a quarter of a century has built the confidence the Medical Profession has in "PURITAN MAID" Medical Gases.

NITROUS OXID ★ CYCLOPROPANE ★ ETHYLENE
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Helium ★ Oxygen & Carbon Dioxid ★ Oxygen

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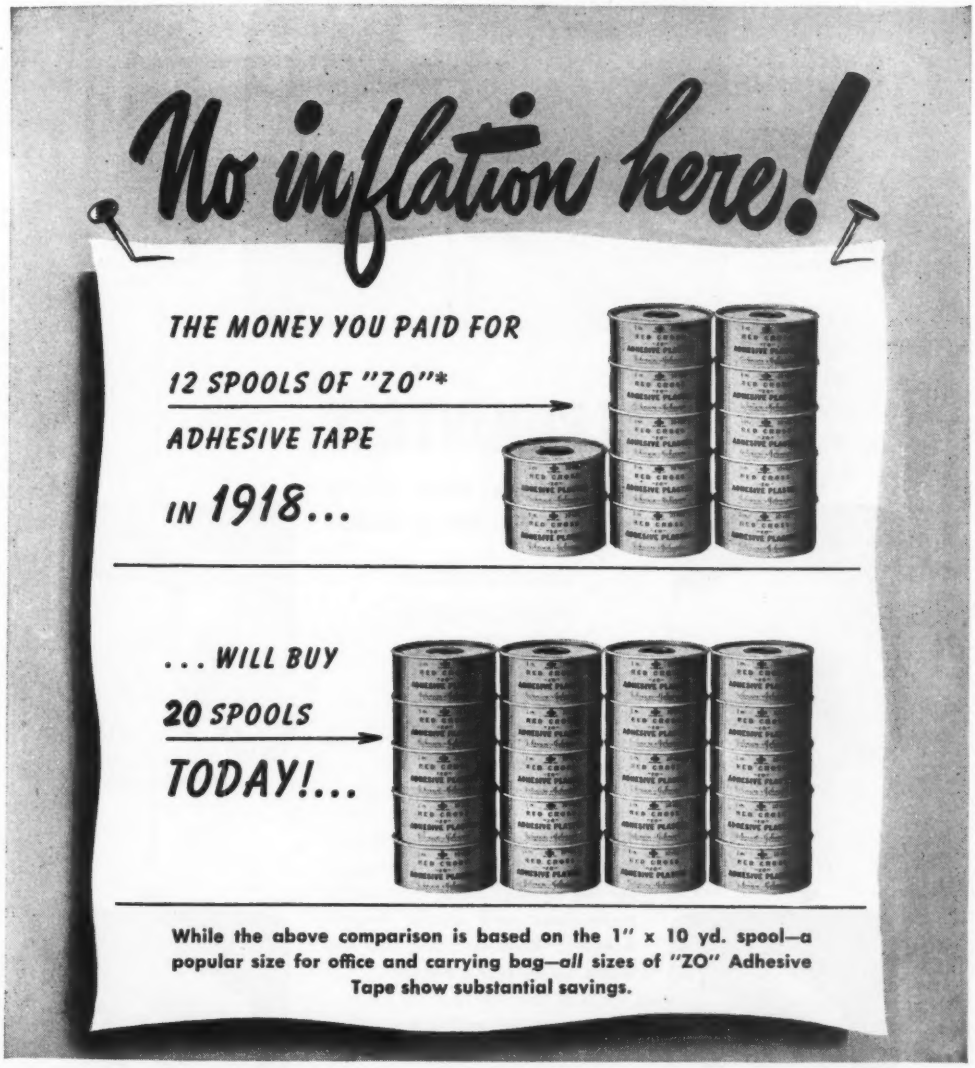
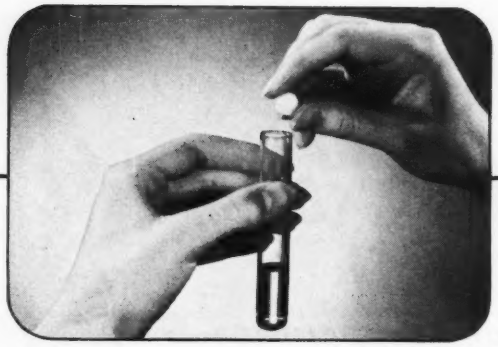

No inflation here!
THE MONEY YOU PAID FOR
12 SPOOLS OF "ZO"*
ADHESIVE TAPE
IN 1918...
... WILL BUY
20 SPOOLS
TODAY!...
While the above comparison is based on the 1" x 10 yd. spool—a popular size for office and carrying bag—all sizes of "ZO" Adhesive Tape show substantial savings.

THIS interesting comparison of "ZO" Adhesive Tape values during 1918 and 1945, is clear evidence of the Johnson & Johnson philosophy of giving you the highest quality products at the lowest possible cost.

Johnson & Johnson
NEW BRUNSWICK, N. J. CHICAGO, ILL.

Trade Mark of product made exclusively by Johnson & Johnson



TURBIDITY METHOD
(1) Drop one tablet in 4 cc. water.

RING METHOD
(1) drop one tablet in 4 cc. water.

ALBUMINTEST

SIMPLE, CONVENIENT TABLET TEST FOR QUALITATIVE DETECTION OF ALBUMIN

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NONPOISONOUS
NONCORROSIVE
NO HEATING

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ADAPTED TO BOTH
TURBIDITY
and RING
METHODS OF TESTING.

Quick, reliable, conveniently carried, Albumintest is designed for use by physicians, laboratory technicians and public health workers. Bulk solutions may be made up in any quantity.

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Economical in bottles of 36 and 100

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ORDER FROM YOUR DEALER

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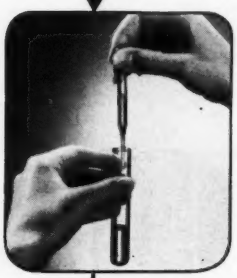
A Companion to Clinitest — Tablet Method for Urine-Sugar Analysis



(2) drop in 1 cc. urine.

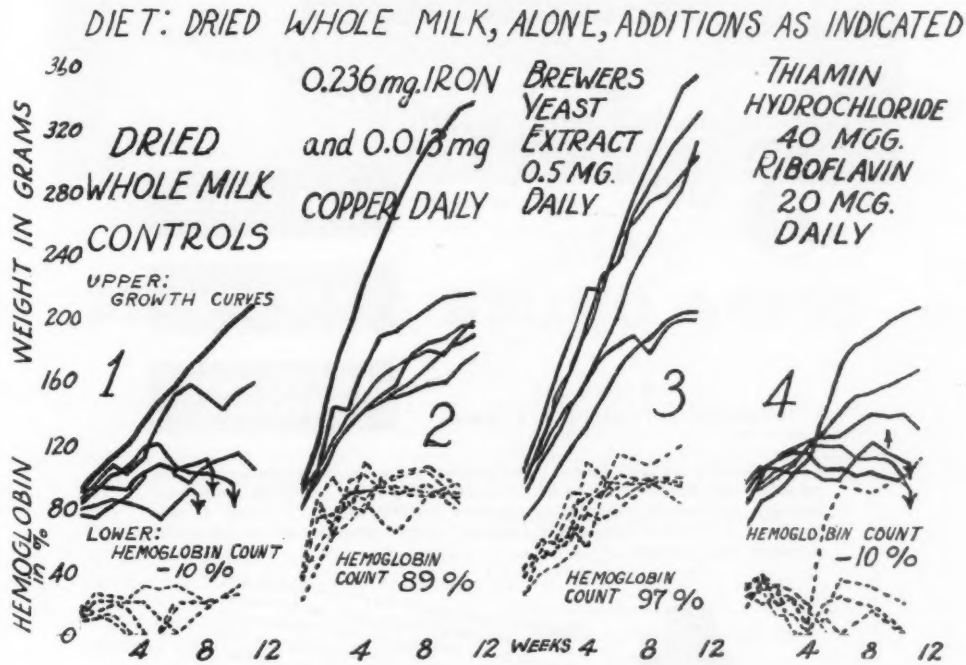
(3) degree of turbidity indicates presence of albumin.

(2) float in 1 cc. urine.

(3) ring density indicates presence of albumin.

AMES COMPANY, Inc., Elkhart, Indiana

From Vitamin Food Company's Research Laboratories



2. Copper and Iron (2) nearly, not quite, protect the hemoglobin, with more growth than had from the Dried Whole Milk. There is no reproduction.

3. Brewers Yeast Extract (3) gives normal growth, a litter and full hemoglobin protection. It is normally high in iron with adequate copper supplement; supplies B Vitamin factors, including the extrinsic anti-anemia factor—not yet separated—in which milk is deficient.

4. Thiamin and Riboflavin (4) added show no value over the Dried Whole Milk Diet. It is an observation of value in supplementing the bottle formula with needed B Vitamins.

Samples sent to physicians and hospitals

VITAMIN FOOD COMPANY, INC.

Vitamin Research Laboratories, Inc.

187 Sylvan Avenue **Newark 4, N. J.**

for more effective

Oral **VITAMIN B COMPLEX THERAPY**

LIPO-HEPLEX

(U. S. VITAMIN)

3 significant Fractions of Liver

AQUEOUS

LIPOID

80% ALCOHOL-INSOLUBLE

. . . combined with

IMPORTANT CRYSTALLINE B VITAMINS

Current laboratory and clinical investigations show that a combination of the aqueous *and* lipoid fractions of liver, providing more complete nutritional therapy, is clinically superior to aqueous extracts alone . . . since certain essential nutritional factors are removed in the preparation of the usual aqueous liver extracts.

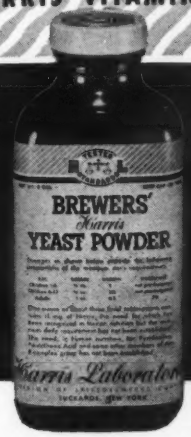
Provides in each capsule the vitamin extracts and concentrate (water-soluble, 80% alcohol-insoluble and lipoid fractions) derived from a total of 11.5 grams of liver . . . including folic-acid fractions (L. casei factor [Bc] etc.), biotin, inositol, and other nutritional factors present in the liver fractions. Each capsule contains:

Thiamine HCl (B_1)	2.0 mg.
Riboflavin (B_2)	2.0 mg.
Niacinamide	10.0 mg.
Pyridoxine HCl (B_6)	0.1 mg.
Calcium Pantothenate	3.0 mg.
Choline	10.0 mg.
Inositol	5.0 mg.
Folic-acid fractions	10.0 mcg.

Professional Samples and Literature

U. S. VITAMIN CORPORATION • NEW YORK 17, N. Y.

HARRIS VITAMINS ARE NEVER PROMOTED TO THE PUBLIC



Complete B-Complex
as found in
NATURAL SOURCE

plus
ESSENTIAL AMINO ACIDS

BREWERS' YEAST POWDER (Harris) with its complete B-complex factors as found in this natural source, plus the essential amino acids, is finding wide usefulness as an accessory to the diet in pregnancy, lactation, postoperative and other convalescent cases, as well as for growing children.

The essential amino acids which BREWERS' YEAST POWDER (Harris) yields, are an important additional factor because after more than a century they still remain the *first* in the regulation of vital processes (growth, formation of enzymes, hormones, and many immunologic and antigenic reactions[1])—and because many modern diets provide insufficient biologically superior protein.[2]

[1]Lewis, Howard B.: Proteins in Nutrition, J.A.M.A. 120:198, 1942.
[2]Wilder, Russell M., and Keys, Thomas E.: Unusual Foods of High Nutritive Value, J.A.M.A., 120:529 1942.

HARRIS VITAMIN PREPARATIONS NOW EMBRACE:

Halabex • Halapan • Haladee
Brewers' Yeast Powder (Harris)
Nicotinic Acid • Vitamin C
Vitamin B_1 • Vitamin B_2

HARRIS QUALITY
Harris Laboratories
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Tuckahoe, N. Y.

PRODUCERS OF VITAMINS
FOR MEDICAL USE SINCE 1919

HARRIS LABORATORIES Dept. S
Tuckahoe, N. Y.
I would like a trial package of Brewers' Yeast Powder (Harris) and information on new HARRIS Vitamin Preparations.

Name_____
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Why GIVE THE DROSS . . .

. . . WHEN ONLY THE GLYCOSIDE PRODUCES THE CARDIAC ACTION

COUNCIL ACCEPTED

ACCORDING to N. N. R.,[1] Digitaline Nativelle—the original digitoxin, in pure, crystalline form—is the chief active glycoside of Digitalis purpurea completely freed from the inert, unabsorbable substances of digitalis leaf. *One milligram* of Digitaline Nativelle produces approximately the same cardiotonic action as *one gram* of U.S.P. XII digitalis.

Since it is completely absorbed on oral administration, it produces the same result whether given by vein or by mouth, and nausea and vomiting due to local irritation are almost never encountered.

In urgent cases—provided the patient has not received digitalis in any form for two weeks—the average dose of 1.2 mg. for initial digitalization can be given safely at one time by mouth and will produce its full therapeutic effect in 3 to 6 hours.[2] The average maintenance dose is 0.1 mg. per day, to be increased or decreased as required.

[1] N.N.R., 1941, page 210.
[2] Gold, H.; Cattell, M.; Modele, W.; Kwit, N. T.; Kramer, M. L., and Zahm, W.: J. Pharmacol. & Exper. Therap. 82:187 (Oct.) 1944.

• • •

Digitaline Nativelle is available through all pharmacies in 0.1 mg. tablets (pink) and 0.2 mg. tablets (white), in bottles of 40 tablets. Also in 0.4 mg. (2cc.) and 0.2 mg. (1cc.) ampuls, in boxes of 6 ampuls, for intravenous use when the oral route cannot be employed.

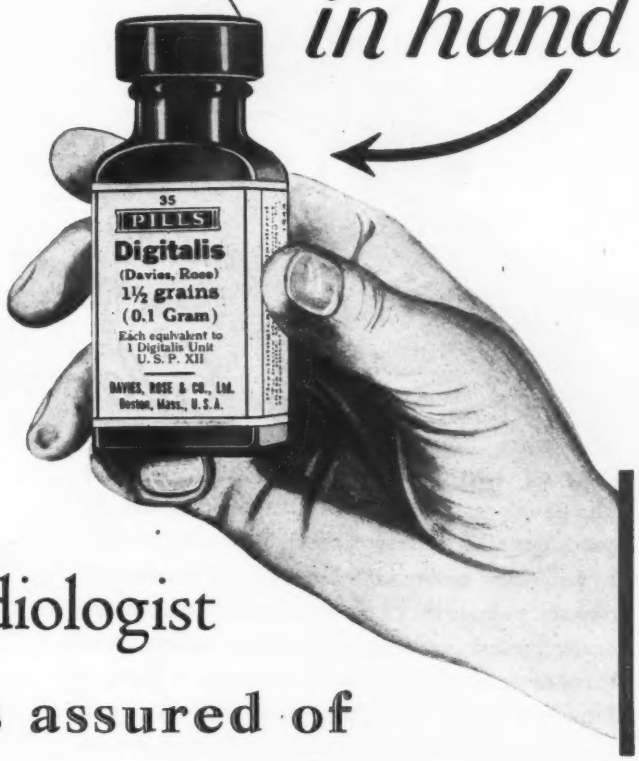
Physicians are invited to send for clinical test sample and literature

VARICK PHARMACAL COMPANY, INC.
A Division of E. Fougera & Co., Inc.
75 Varick Street, New York 13, New York

Digitaline Nativelle
REG. U. S. PAT. OFF.

THE ORIGINAL DIGITOXIN, IN PURE, CRYSTALLINE FORM

With this in hand



The Cardiologist

is assured of

Dependability in Digitalis Administration

• • •

Being the powdered leaves made into
physiologically tested pills,
all that Digitalis can do, these pills will do.

Trial package and literature sent to physicians on request.

DAVIES, ROSE & COMPANY, Limited

Manufacturing Chemists, Boston 18, Massachusetts

D14

PALATABLE • WELL TOLERATED • THERAPEUTICALLY EFFECTIVE

The development of CALCREOSE (Maltbie) has, indeed, "smoothed the rough spots" in creosote therapy so frequently provocative heretofore of nausea and distress. • Moreover, CALCREOSE (calcium creosotate) exerts bactericidal and bacteriostatic action up to *three times as great* as that of creosote. • Thus, in providing all the well-known benefits of creosote in a *pleasant* and *palatable* form, CALCREOSE proves highly effective in many bronchial and respiratory affections . . . lessening cough, diminishing expectoration, reducing its purulency and deodorizing sputum. Also it tends to stimulate the appetite and improve the patient's general condition.

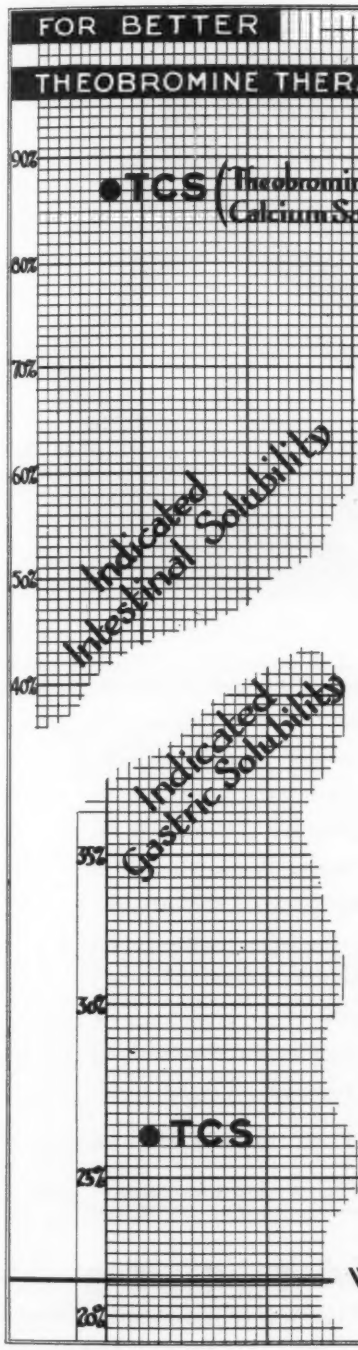
AVAILABLE: As tablets (4 gr.) in bottles of 100, 500, and 1000. COMPOUND SYRUP CALCREOSE in pint or gallon bottles.

Calcreose

THE MALTBIE CHEMICAL COMPANY • NEWARK, NEW JERSEY

FOR BETTER

THEOBROMINE THERAPY



TCS

Each Tablet Contains:

Theobromine Salicylate	6 grs.
Calcium Salicylate	1 gr.
Phenobarbital	¼ gr.

T C S offers theobromine in the form of the superior "true salt"--- Theobromine Salicylate, with solubility protected by calcium salicylate. Carefully controlled laboratory research indicates that the solubility of the theobromine in T C S is low in gastric environment and exceptionally high in intestinal environment. T C S is consequently better tolerated gastrically and is superior in absorbability and efficiency.

The dosage of T C S in hypertension, angina pectoris, and following partial recovery from coronary occlusion is one tablet three or four times a day.

WM. P. POYTHRESS & CO., INC.
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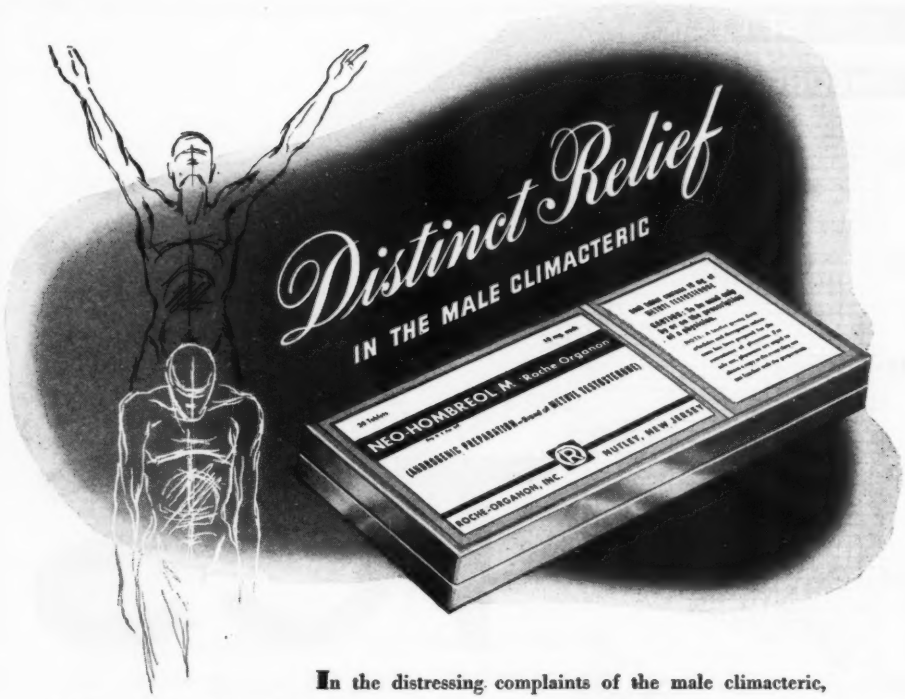

In the distressing complaints of the male climacteric, "therapy with androgenic substances has given distinct relief" (1). Following adequate male hormone therapy patients experience rapid improvement of such disagreeable symptoms as nervousness, irritability, emotional instability, mental and physical fatigue, decreased libido and potency, and other complaints due to the male climacteric. In the treatment of disorders due to male hormone deficiency, "oral medication with methyl testosterone has proved satisfactory" (2). Neo-Hombreol (M) tablets, the Roche-Organon brand of methyl testosterone, are preferred by many physicians for the treatment of the male climacteric, since they offer the advantages of therapeutic efficacy, convenient administration and worthwhile economy. Neo-Hombreol (M) tablets, 10 mg, are available in boxes of 15, 30, and 100. For parenteral administration, Neo-Hombreol (testosterone propionate) is available in 1-cc ampuls in 3 strengths: 5, 10, and 25 mg.

ROCHE-ORGANON, INC., ROCHE PARK, NUTLEY 10, NEW JERSEY

(1) Editorial, *J.A.M.A.*, *126*:300, 1944; (2) Council of Pharmacy and Chemistry, *J.A.M.A.*, *125*:788, 1944

NEO-HOMBREOL (M) Tablets
'ROCHE-ORGANON'

"FIGHT INFANTILE PARALYSIS • JANUARY 14th—31st"

Pioneers in Shock Therapy Selective

For Southern Physicians whose Psychoneurotic and other Psychopathologic Patients require Specialized Treatment in Scientific Psychiatry suitable to their individual needs.

We do not treat narcotic addictions or acute alcoholic intoxication.

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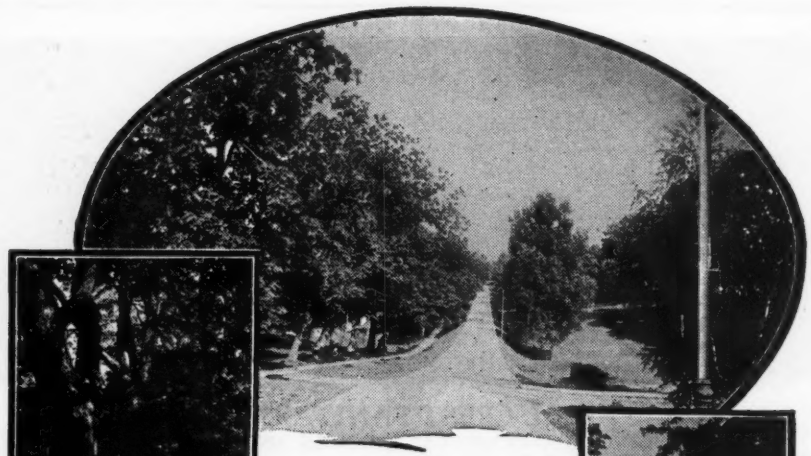

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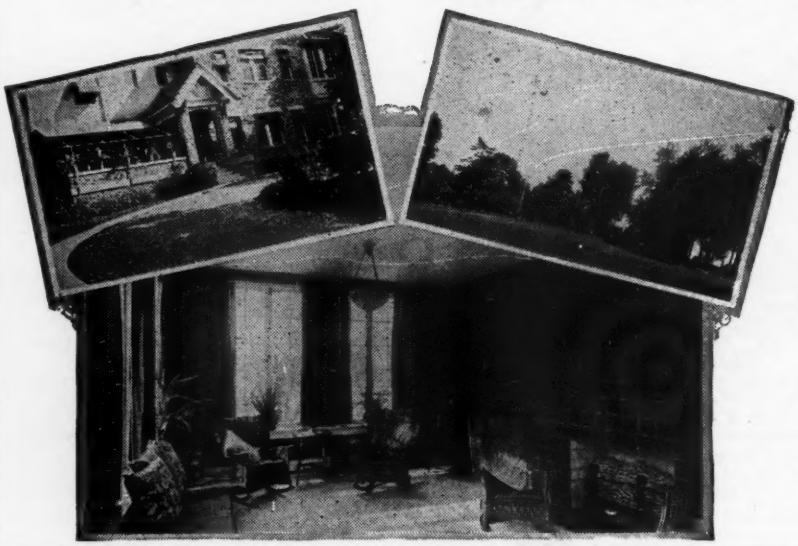

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JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 38 NOVEMBER 1945 Number 11

OBSERVATIONS OF THE ANTI-ANEMIC PROPERTIES OF SYNTHETIC FOLIC ACID*

By TOM D. SPIES, M.D.,
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MARY B. KOCH, B.A.,
and
MARGARET H. CALDWELL, B.S.
Birmingham, Alabama

Minot, Castle, and others[1 2 3] have clearly described the phenomenon of reticulocytosis as a part of the remission of Addisonian pernicious anemia following administration of therapeutically effective substances. Increased numbers of reticulocytes in the peripheral blood have been reported to occur following administration of arsenic,[3] congo red,[4] pyridoxine,[5] and other nonspecific substances. This type of response is not followed by the characteristic rise in hemoglobin and red blood cells, important in the remission of relapsed macrocytic anemia.

The high incidence of macrocytic anemia found among patients in the Nutrition Clinic, Birmingham, Alabama, has stimulated not only a study of the natural history, morphology, and etiology of the disease,[6] but has also offered opportunity for study of reticulocytosis and erythrogenesis. Consequently, numerous substances have been tested in collaboration with Drs. C. V. Moore, R. W. Vilter, C. A. Doan, W. B. Bean, N. L. Brookens, and H. S. Collins, and the effects noted on the clinical progress of the patient, on reticulocytosis, leukocytic equilibrium, and red cell and hemoglobin regeneration. The substances tested included niacin, thiamin, riboflavin, calcium pantothenate, pyridoxine, inositol, para-aminobenzoic acid, choline, pyridoxamine, and pyridoxal. They were found to be of little or no efficacy in treating this type of anemia. Crude folic acid concentrates have likewise yielded no specific hematological response. Ascorbic acid was observed to cause reticulocytosis and sometimes blood regeneration in selected cases.

While fractionating reticulogen, Dr. J. K. Cline has isolated several materials of unknown structure which, when given parenterally to patients with macrocytic anemia, have produced reticulocytosis of varying degree. Rises as high as 10-12 per cent in some instances have not been associated with positive evidence of regeneration, but in others, brief and minimal rises in the reticulocytes have been followed by rather remarkable regeneration of red cells, white cells, and hemoglobin.

The reticulocytosis which occurs following the administration of a synthetic substance, Lactobacillus casei factor, considered a part of the B complex, is of such interest as to warrant this report.

The synthesis of the L. casei factor has been announced by sixteen investigators[7] at the Lederle Laboratories and the Calco Division of the American Cyanamid Company. The Lederle Laboratories supplied the material for clinical trial. It is described as active for L. casei, S. faecalis R, and as promoting growth and hemoglobin formation in the chick. L. casei factor, dissolved readily in saline made alkaline with small amounts of sodium bicarbonate, was given

*Received for publication September 18, 1945.

*University of Cincinnati Studies in Nutrition at the Hillman Hospital, Birmingham, Alabama. From the Department of Internal Medicine, University of Cincinnati College of Medicine.

*These studies were supported by grants from the Nutrition Foundation, Eli Lilly and Company, and Lederle Laboratories.

Valuable nursing care was afforded by Miss Monette Springer, R.N., and Miss Betty Duncan, R.N., who also assisted us in the dietary control of the patients.

intravenously to five subjects with macrocytic anemia in relapse. All of the patients were admitted to the hospital during a control period and during therapy. The diet was rigidly controlled eliminating meats and meat products. Three of the patients had in the past been treated with liver extracts by the authors with a satisfactory hematological response. A fourth had had a remission in the previous year following treatment with liver extract by a private physician. The fifth had never been treated with liver. Daily examinations of the blood were made including erythrocyte and leukocyte counts, hemoglobin determinations (using a photoelectric colorimeter), and reticulocyte counts. Reticulocytes were stained by the wet method, using an aqueous preparation of brilliant cresyl blue.

Similar to the subjective sensation that comes upon the patient with macrocytic anemia in relapse several days after liver extract, these patients felt a definite upsurge of well-being three or four days after the first injection. The results of the injection of L. casei factor on the reticulocyte percentages are shown in *Table 1.*

EFFECT OF PARENTERAL ADMINISTRATION OF FOLIC ACID

	Initial		Reticulocytosis			Duration of	
Case	Millions Red Cells	Hg. Gm.	First Day of Rise	Day of Peak	Per Cent at Peak	Administration (days)	Total Dose Mg.
1	1.82	7.7	4	6	10.6	1	50
2	2.54	8.7	4	7	9.0	1	20
2a	2.15	8.8	4	8	14.8	18	360
3	1.61	6.2	8	10	11.0	18	360
4	1.90	9.2	6	8	14.5	14	280
5	1.95	7.0	6	8	6.5	13	260

Table 1

Cases 1 and *2* were given single injections of the substance, and the subsequent reticulocyte rise subsided eleven days from the time of injeetion. *Cases 3, 4,* and *5* were given 20 mg. L. casei factor intravenously daily for 18, 14, and 13 days. On this regime the rise was more sustained. A slight increase in the number of red blood cells and hemoglobin content occurred in each case.

Ten days after the reticulocytes fell to the control level in *Case 2* (following the single injection), 20 mg. L. casei factor was again injected, on this occasion intramuscularly and at daily intervals. Reticulocytes again increased, reaching a peak of 14.8 per cent on the eighth day. This response is noted in the table under *Case 2a.*

The amount of material available to us was small, however, and when more became available, we decided to administer it by mouth to four additional persons with macrocytic anemia in relapse. Three of them were given 50 milligrams twice a day, and the fourth was given 50 milligrams three times a day. They all responded promptly, as seen in *Table 2.*

EFFECT OF ORAL ADMINISTRATION OF FOLIC ACID

	Millions Red Cells		Hemoglobin Gm.		Reticulocytosis		
Case	Initial	Twelfth Day	Initial	Twelfth Day	First Day of Rise	Day of Peak	Per Cent at Peak
6	1.64	3.21	7.1	9.7	4	5	19.2
7	2.01	3.10	9.2	10.2	5	8	10.0
8	2.01	2.69	8.3	10.0	3	5	19.8
9	2.35	3.35	7.8	9.1	4	7	21.4

Table 2

It is obvious from the results shown in these tables that persons with macrocytic anemia in relapse have a significant hemopoietic response following the administration of synthetic folic acid. This response follows either parenteral injection or oral administration (of course, cases will be found that do not absorb satisfactorily from the alimentary tract, and they will not respond). In every instance the number of reticulocytes increased in the peripheral blood, and the red blood cell counts and hemoglobin content rose toward normal levels.

Studies directed toward determining more of the effects of L. casei factor on the regeneration of hemoglobin and erythrocytes are underway in this Clinic.

BIBLIOGRAPHY

1. Minot, G. R.; Murphy, W. P.; Cohn, E. J.; Stetson, R. P.; and Lawson, H. A.: The Feeding of Whole Liver or an Effective Fraction in Pernicious Anemia: The Response of the Reticulocytes. Transactions of Association of American Physicians, 42:83, 1927.
2. Minot, G. R.; Murphy, W. P.; and Stetson, R. P.: The Response of the Reticulocytes to Liver Therapy: Particularly

in Pernicious Anemia. Amer. J. Med. Sci., **175**:581-599, 1928.
3. Minot, G. R.; and Castle, W. B.: The Interpretation of Reticulocyte Reactions. Lancet, **2**:319-330, 1935.
4. Massa, M.; and Zolezzi, G.: Minerva Med., **2**:763-771 (Dec. 1) 1934; also, Klin. Wchnschr, **14**:235-237 (Feb. 16) 1935. Cited by Mermod, C., J. Clin. Investiga., **15**:559-569, 1936.
5. Vilter, R. W.; Shiro, H. S.; and Spies, T. D.: The Effect of Synthetic Vitamin B_6 on the Hemopoietic System of Human Beings. Nature, **145**:338, 1940.
6. Moore, C. V.; Vilter, R.; Minnich, V.; and Spies, T. D.: Nutritional Macrocytic Anemia in Patients with Pellagra or Deficiency of the B Complex. J. Lab. and Clin. Med., **29**:1226-1255 (Dec.) 1944.
7. Angier, R. B.; Boothe, J. H.; Hutchings, B. L.; Mowat, J. H.; Semb, J.; Stokstad, E. L. R.; SubbaRow, Y.; Waller, C. W.; Cosulich, D. B.; Fahrenbach, M. J.; Hultquist, M. E.; Kuh, E.; Northey, E. H.; Seeger, D. R.; Sickels, J. P.; and Smith, J. M., Jr.: Synthesis of a Compound Identical with the L. casei Factor Isolated from Liver. Science, **102**:227-228 (Aug. 31) 1945.

URINARY CALCULOSIS AS A PHASE OF CRYSTALLINIZING PYELONEPHRITIS*

By LINWOOD D. KEYSER, M.D.
Roanoke, Virginia

Research in the field of urinary lithiasis has after a period of two decades of rather brilliant productive activity lapsed into a fallow period. It is the purpose of this study to review the broader aspects of the whole problem from a clinical and experimental standpoint and to undertake to uphold the thesis that stone formation usually begins with calcification or crystallinization of impaired surface epithelial tissue. It grows to the proportion of a true calculus when such crystallinized epithelium is exposed to the free urinary stream. The effort will be made to demonstrate that such tissue calcification or crystallinization is related to and obeys what we know of the laws of tissue calcification in general.

The complexities of crystalline deposition in tissues are as yet too little known in spite of a voluminous literature on ischemia, acid-base disturbances, the action of enzymes, the hydrolysis of fats and the formation of calcium soaps and many other highly hypothetical etiologic factors. McCallum's law that calcification takes place in dying tissue which is embedded in and surrounded by tissue accessible to circulating fluids, seems to epitomize our concrete tangible knowledge of the subject.

*Read in Section on Urology, Southern Medical Association, Thirty-Eighth Annual Meeting, St. Louis, Missouri, November 13-16, 1944.

Likewise the phenomenon of precipitation of crystalline matter from supersaturated colloidal solutions has been perhaps overworked and overexplained without too much of pragmatic or utilizable knowledge having been given us by physical chemists.

Let us approach the problem from a different point of view, leaving aside the purely physicochemical concepts of colloidal solutions for the moment. The several varieties of calculus formation experimentally produced and correlated fairly consistently with clinical findings are stones produced by avitaminosis, stones produced by crystalline hyperexcretion, stones arising in areas of aseptic degenerative changes in the kidney and perhaps occasionally in the bladder, ureter or prostate, and finally stones produced by bacterial action in the urinary tract, i.e., stones of infection.

Do such calculi arise from precipitation of crystalline matter from the free urinary stream and unattached directly to urinary tract epithelium or do they originate in the epithelium as part and parcel of its substance? We shall review the evidence and let it speak for itself.

AVITAMINOSIS STONE

Avitaminosis stone produced experimentally in several species of animals by dietary deficiency in vitamins A and D shows the following sequential features in its pathology as described by Grossmann[1] and others.[2-10] On such dietary, animals show, first, a degenerative change in the general epithelium of all body structures. This reaches ultimately a high degree in the urinary tract epithelium where keratinization and desquamation takes place. The urine becomes intensely alkaline and a general breakdown in the epithelium of the renal tubules especially in the pyramids, is associated with deposition of lime salts within and upon this epithelium. Clinically we have no correlated pathologic study of the human organism with this feature in mind although certain studies of McCarrison[2] are suggestive. Thus at the outset we see a degenerative nephritic lesion with secondary crystalline deposition in areas exposed to the urinary stream as the cardinal feature of avitaminosis stone.

HYPEREXCRETION STONE

In studies of calculi produced experimentally with oxamide, calcium oxalate, and calcium carbonate feeding in various species, we find in the early stages that the collecting tubules of the pyramid are clogged with crystalline material. In the beginning of my own studies I personally was much more impressed with the studies of urinary sediments in such animals. These showed a change in crystalline form from isolated crystals to those of spherical fusing forms. In consequence I felt that such spherical clusters being precipitated in gelling colloid from the urine after its secretion and excretion from the papilla, would form the nidus of a growing calculus, if these crystalline clusters were caught and held by mere adhesion due to surface tension forces to the crypts in the depth of a calyx. Following Randall's work[3] and his description of type 2 lesions I made a review of the subject. This brought much doubt as to the frequency of stone deposition from the free urinary stream. It was found that the clogging or inspissation of crystals in the tubules was associated with a nephritic tubular epithelial degenerative change which long preceded any crystalline deposition. Furthermore in oxamide and oxalate hyperexcretion we could trace microliths growing off the tips of the papillae both in gross and microscopic sections. Also cloudy swelling and degenerative changes and a lesser degree of crystalline deposition was noted in the proximal tubular structures and to some extent these depositions were noted even in the glomerular zones. Here again in the terminal collecting tubes at the pyramidal tips the epithelium itself seemed to be impregnated with crystalline matter and to become itself a part of the embryonic stone structure. This crystallinized epithelium at the tip of the pyramid becomes the site of attachment, the point d'appui from which the stone will grow as crystals are further deposited

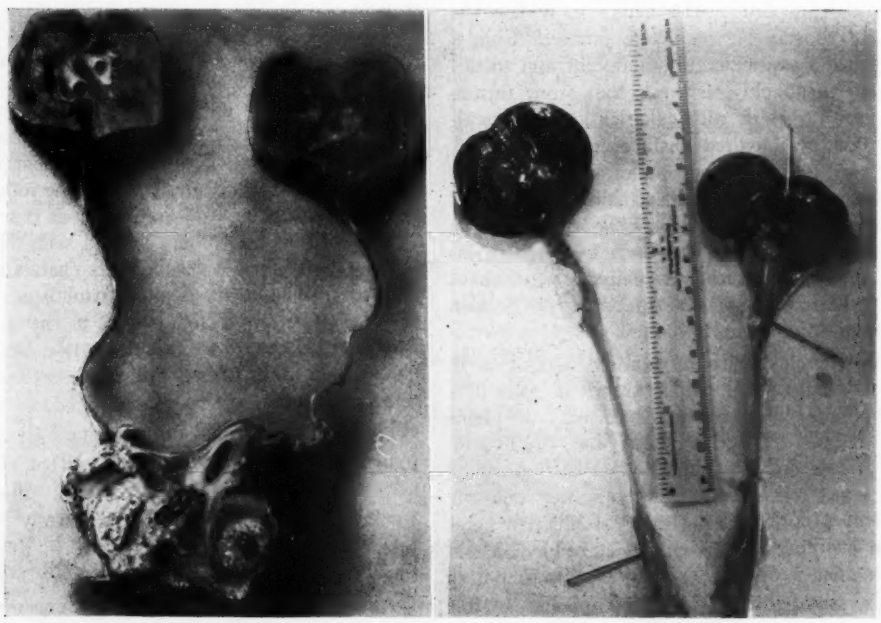

Fig. 1

Calcium oxalate hyperexcretion calculosis in rabbit (*left*). Calcium carbonate hyperexcretion calculosis in rabbit (*right*). Note stones in bladder only in oxalate experiment but pyramids are streaked with inspissated calcium oxalate crystals. In calcium carbonate experiment small calculi are attached to pyramids which are filled with inspissated crystalline matter. Small stones and calcareous deposits along ureter.

upon it from a supersaturated urine with which it is constantly in contact. Free particles of precipitated crystals will sooner or later be washed away and passed with the urine. This is consistently the fate experimentally when finely powdered oxamide stone is placed into the animal kidney pelvis directly through incisions. (*Figs. 1, 2* and *3.*)

Again, if we place a piece of muscle tissue or a section of renal papillary tip into the rabbit's kidney, we can trace the degeneration of this material through several experimental sequences. If the urine is alkaline a certain amount of crystalline calcium deposition is noted after a few weeks in the surface of such tissue. If oxamide is fed the oxamide crystals become intimately attached to this foreign degenerating tissue and impregnate its surface. If feeding is continued a large calculous mass is produced. The crystalline impregnated tissue lies at its center and becomes its nucleus as may be demonstrated microscopically. (*Fig. 4.*)

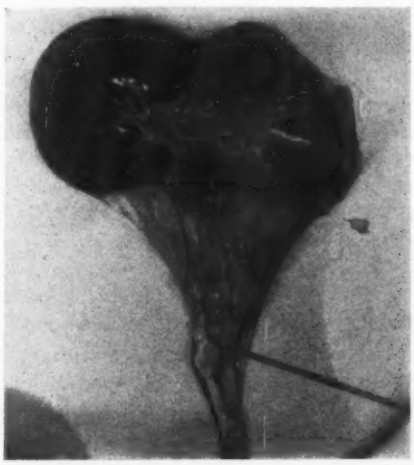

Fig. 2

Calcium carbonate hyperexcretion calculosis in rabbit. Slightly enlarged to show detail of calcified pyramidal tips at terminus of collecting tubules.

From the clinical side the evidence of nephritic change in hyperexcretion calculosis is likewise noted. In hyperparathyroid disease aseptic chemical nephritis with an amorphous crystalline tubular deposition is a prominent feature. This is also true to some extent, as yet not accurately determined, in gout or hyperuricacidemia where uratic calculi are found in a variable but not consistent degree. Hench[4] found uratic calculi in 12 per cent of 100 patients with gout, a figure not inconsistent with the occurence of calcium stones in hyperparathyroid disease.

Nephritis of a similar type is found also in sulfonamide lithiasis. Here spiculated crystals of acetylated sulfonamide clog the urinary tubules, produce hemorrhagic areas of tubular degeneration, with deposition of these crystals therein to become a precursor of small calcareous aggregates. These small epithelial calcareous aggregates become detached in part or in whole to grow in stasis areas near the calyces. Ultimately they become stones. Sulfonamide lithiasis simulates in many chemical and histologic details that produced experimentally by oxamide.

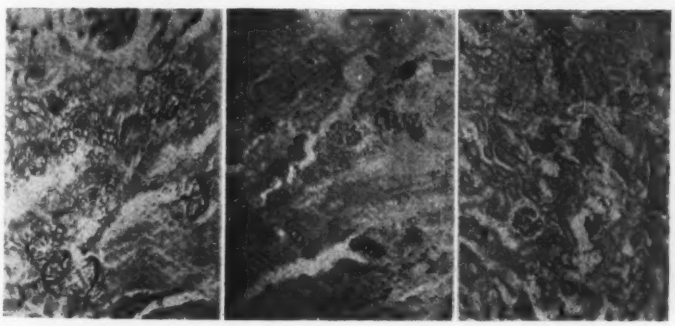

Fig. 3

Experimental hyperexcretory calculosis (calcium oxalate) in rabbit. Note tubular nephritis with massive crystalline deposition within and upon necrobiotic epithelium. Tubular inspissation more intense near papillary tip (*left*).

INFECTIOUS CALCULOSIS

In infectious lithiasis the concept of a crystallinizing pyelonephritis as the basis of the morphogenesis of stone again becomes apparent both in animal experimentation and in pathologic studies. The introduction of urea-splitting

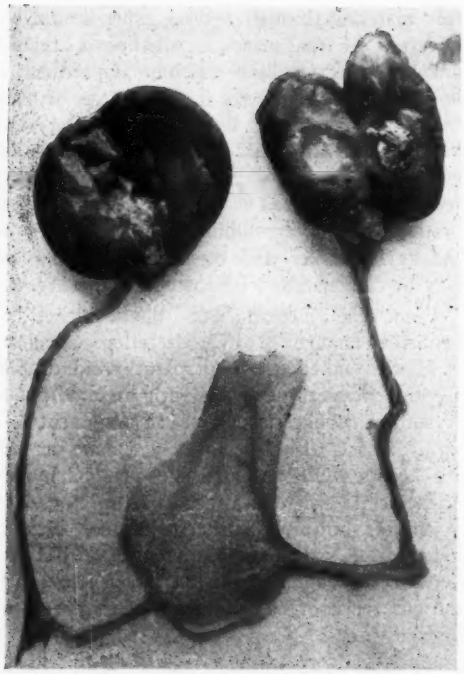

Fig. 4

Piece of muscle tissue placed surgically in rabbit's left kidney. Animal fed on oxamide. After several weeks the tissue becomes impregnated with crystals and a large calculous mass is found. The crystalline impregnated tissue becomes the center of the stone.

organisms into the animal urinary tract will not produce calculus unless previous or concomitant trauma is present. The trauma necessary in experimental animals is definite and of considerable degree. Introducing 1-1000 salicylic acid solution in alcohol into the rabbit's bladder causes an intense chemical cystitis. Superficial epithelium is destroyed, the nuclei disappear and shadows of dying cells remain. Now introduce, after a few days, a culture of type-specific urea splitting proteus or streptococcus and we develop a type of bacterial inflammation that will produce calcium carbonate deposition in the surface cells. In further stages of this process alkaline encrusted cystitis ensues. Then fragments break off to produce stones. This is one of the earliest and one of the simplest types of experimental infectious calculosis, first carried out by Hegar and Magath,[5] and later independently confirmed by myself[11] and Davolos[6] in subsequent studies. (*Fig. 5.*)

Now we may expose the kidney directly and traumatize its pyramids by electrocoagulation or by local injection of alcohol or mercuric chloride. If we then inject directly into this traumatized area several minims of a urea-splitting proteus culture, calculosis at this site will develop after a few weeks. At first the site of this stone formation will be localized to the

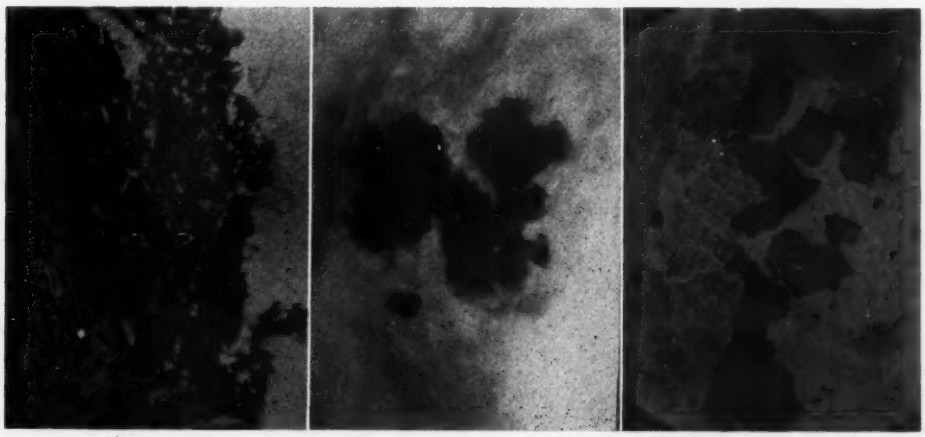

Fig. 5

Infectious lithiasis in rabbit's bladder. Von Kossa Stain. (*Left*) Chemical cystitis (produced by alcohol-salicylic acid solution), necrobiotic epithelium, with early encrustation after infection with urea-splitting proteus. (*Center*)—Calcium carbonate mass growing from bladder wall. (*Right*) Calcium carbonate encrustation at further stage of development. Alkaline encrusted cystitis and free concrements were noted grossly.

traumatized area but later the process involves much of the peripelvic epithelial structure. It then invades the ureter and the bladder mucosa on the treated side. No calculus production however takes place on the other untreated side. At every site involved we find that macroscopically and microscopically the calculous growth begins by calcification of the surface epithelium and that stone growth begins at a point where such calcified epithelium is exposed to the urinary stream. (*Fig. 6.*)

PRODUCTION OF CALCULI BY BACTERIAL TOXINS

The work of Helstrom[7] and of Hryntshak[8] who produced calculi in animals by intravenous injection of staphylococci as well as the production of calcium plaques by intravenous injection of a staphylococcus toxoid by Randall are noteworthy. My own efforts in this field were after many years rewarded by the results of the following study. From a woman of 68 years, with bilateral lithiasis, a green producing Bacillus pyocyaneus was grown. This was not urea-splitting. However, intravenous injection of its culture killed rabbits even in very small doses by producing hemorrhagic tubular nephritis with miliary abcesses and tubular degeneration. In the collecting tubules and pyramids the destructive process attained the magnitude of infarction. We then used minute amounts of a d-brain broth culture and later older cultures which had been treated with a strong alkali and then with a strong acid (NaOH and HCL) and finally brought back to neutrality. With this material we were able to keep six rabbits alive on daily intravenous injections of a few minims over a period of six weeks. These animals were fed on a diet rich in cal-

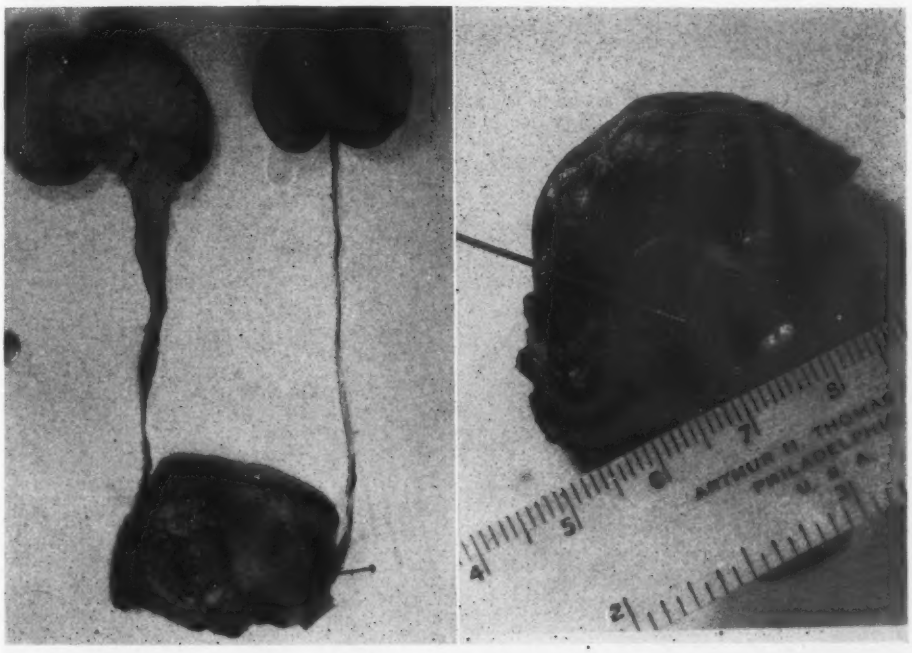

Fig. 6

(*Left*) Unilateral calcareous pyelo-uretero-cystitis. The right kidney was perforated with a needle and electrocoagulation current momentarily applied. B. proteus (urea splitting) culture was inoculated at the Coagulation site. After several weeks massive calculosis in the pelvis, right ureter and area of bladder adjacent to the right ureteral meatus, has formed. The calcium carbonate concretions grow from off the surface epithelium. The left side (untreated) is clear of calcific deposit.

(*Right*) Stone arising in pelvis of rabbit's kidney. Local necrosis produced by hypodermic injection of alcohol-bichloride mixture followed in one-half hour by injection of B. proteus.

cium. However the calcium fed was not in the enormous quantity necessary to produce hyperexcretory stone. All of the six animals developed calcification of the pyramidal tips and microliths. Two developed distinct calculi several millimeters in diameter, lying in the calyceal crypts.

We next made a filtrate of this pyocyaneous

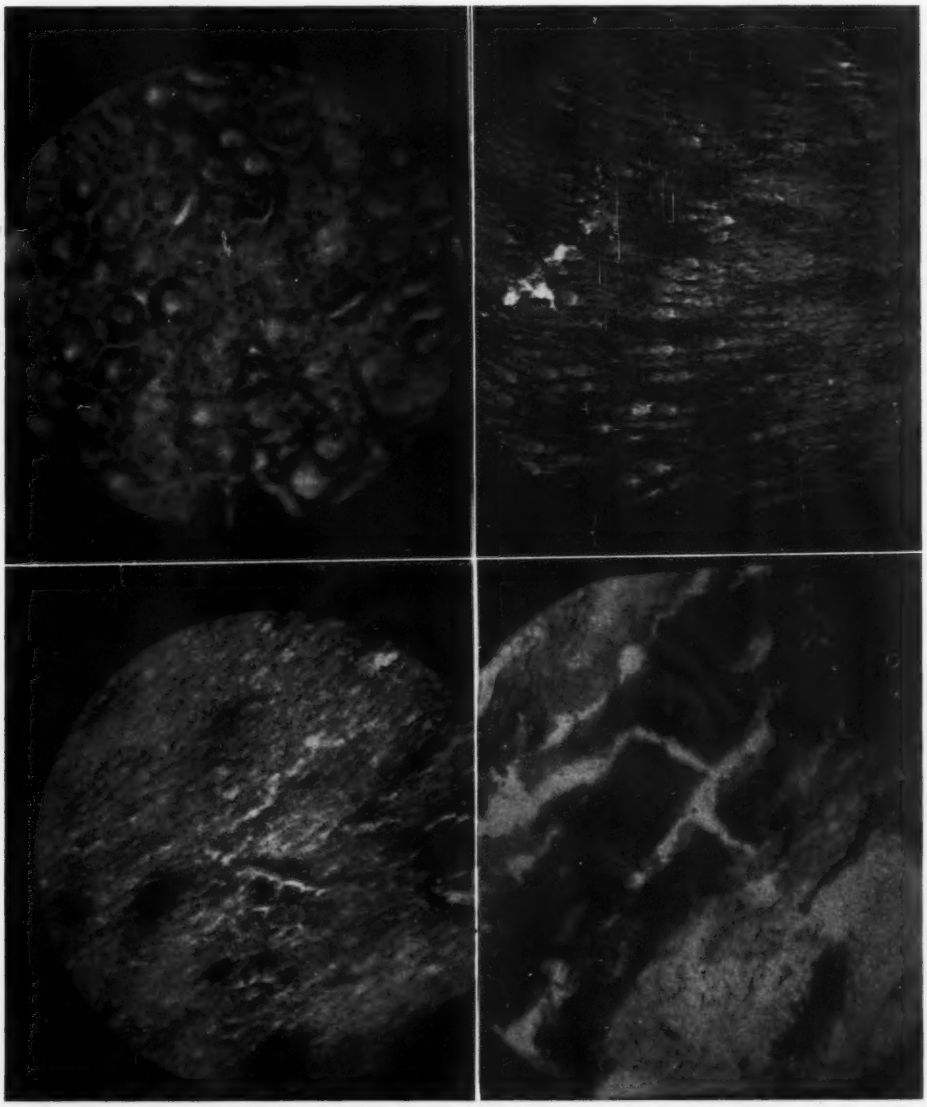

Fig. 7

Hemorrhagic nephritis with cloudy swelling in proximal tubular area, and necrosis towards pyramid (distal tubular system). Lower illustrations (Von Kossa Stain) show progressive calcium phosphate-carbonate deposition. Lesion produced by daily intravenous injection of diluted pyocyaneus culture and filtrate from stone-forming patient.

culture by using the acid-base treatment technic then bringing the material back to neutrality and inactivating it by sterilization with chemicals or heat. Finally the medium was filtered. This material proved highly toxic. However in extreme dilution (1-1000), graded doses were given intravenously daily to rabbits. Aseptic nephritis with terminal tubular calcification ensued. In two instances after several weeks microliths were found attached to the calcified epithelium of the terminal tubules. The small stones were of course found to be composed of calcium phosphate and carbonate. Thus we have an excellent demonstration of the affinity of certain bacteria and of their toxins for the renal tubular epithelium. Calcification and lithifaction with formation of minute calculi followed. The experimental picture of stone formation in a calcifying pyelonephritis was thus achieved. (*Figs. 7* and *8.*)

PATHOLOGY OF STONE-FORMING KIDNEY

The evidence from pathologic studies of the human kidney with calculous disease as observed at operation or autopsy gives further support to the concept of a precedent nephritic lesion with secondary crystalline deposition as the process of stone formation.[9] In many such kidneys I have, over a period of years, studied the histologic patterns of areas adjacent to the stone and in areas more remote. These patterns are varied; but in general, as one would expect, the inflammatory process is more pronounced in the area surrounding the stone, for example, a calculus lying embedded in a minor calyx. This stone-encircling area is composed of fibrotic tissue with round cell infiltration, sometimes hyalinized. If sections from this tissue are stained with Von Kossa silver nitrate technic, we find a marked degree of calcium deposition within and upon the degenerating tissue cells, partly epithelial, partly fibrous, and partly fat. Farther away from this zone surrounding the calculus, a more diffuse pyelonephritis is found, with changes in the intertubular and interstitial areas and with a definite but lesser degree of calcium deposit consistently present. The more intense and the more extensive the lesion, as in advanced proteus infection, the more calcification do we find in the renal parenchyma. This

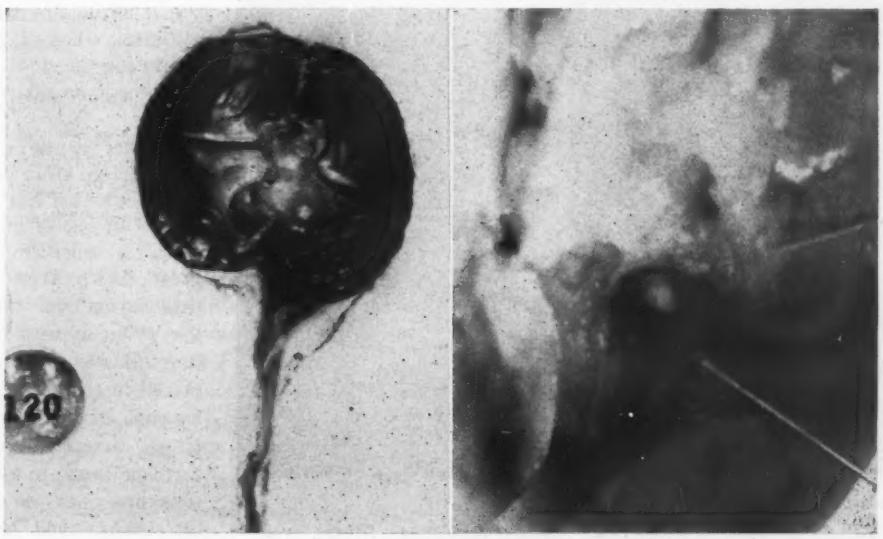

Fig. 8

Small concrements (*left*) in rabbit's kidney after six weeks daily injection of dilute B. pyocyaneus culture and specially prepared toxin. Magnified illustrations of calcification at pyramidal tip and stone lying in calyx (*right*). This is the result of the hemorrhagic tubular nephritis shown in *Fig. 7.*

calcific deposition extends at times to a minor but definite degree to the proximal tubular structures and even to the glomerular zone. The histologic patterns while varied are in every respect similar to those in the experimental animal. From the pelvic surface of the papillary structures, we can trace the evolution of calcific deposit from epithelial impregnation on to true outgrowths which are to become calculi loosely attached to or lying free in a calyx. (*Fig. 9.*)

Another feature of stone-forming pyelonephritis is a frequent lipoid degeneration with replacement lipomatosis in the renal structure and the deposition of lime salts in this fat. This has been especially noted in certain kidneys with large stag-horn or coral calculi which fill the pelvic contours. This calcifying lipomatosis of the kidney is well brought out with a combination of silver nitrate and fat stains and suggests that one of the chemical mechanisms at work at times may be the deposit of calcium in fatty degeneration of tissue. We have seen almost all the parenchyma replaced with fat containing multiple stones surrounded only by a fibrotic ring of tissue separating the stone from the lime-impregnated fat itself.

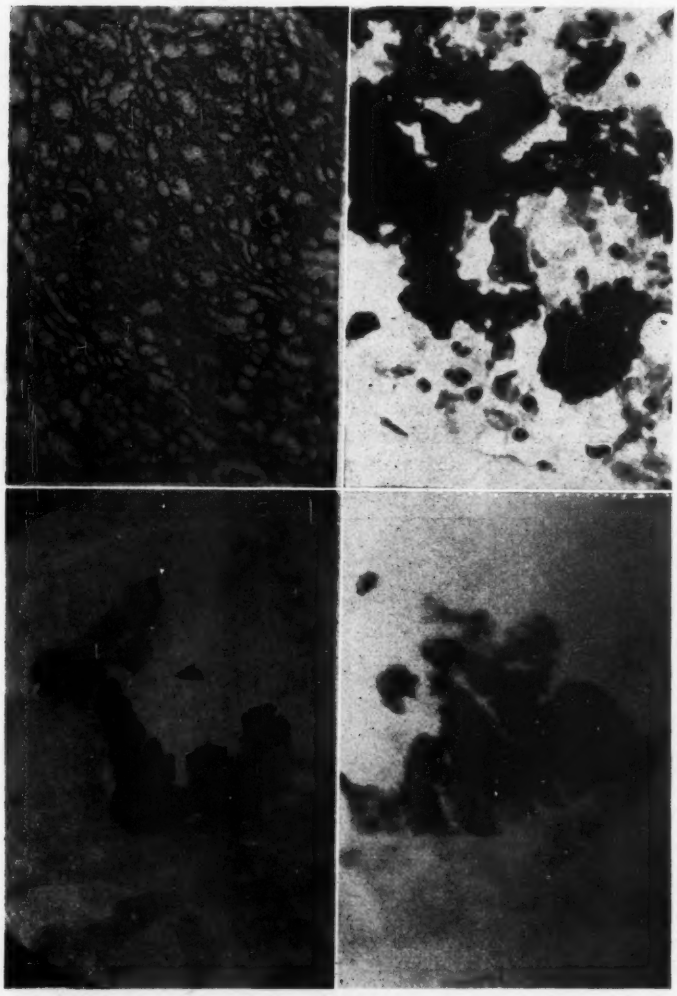

Fig. 9

Histogenesis of calculus in human kidney. Proteus (urea splitting) infection. Von Kossa Stain. (*Upper left*) Calcium phosphate deposit in small amount in area remote from surface. (*Upper right*) Calcium deposits within and upon cells in area adjacent to surface surrounding stone.

(*Lower left and right*) Calcified epithelial masses growing from surface of pyramid and projecting into calyx.

Another type of calcium deposition simulating bone formation has been noted. In one of my patients a calcified mass grew down from the parenchyma and entered the pelvic-ureteral juncture. It was densely attached to the pelvic wall. Sections showed a histologic picture of pseudocartilage and bonelike structure, but no true osteoblasts could be determined.

Thus we see that in certain types of nephritis,

crystalline deposition may occur in polymorphic forms. The calcified areas in neoplasms, the uratic infarcts in infancy, the uratic showers of calculi in gout, the calcified pyramids of the nephrocalcinosis associated with low serum phosphorus, normal serum calcium, and hyperchloridemia are other examples that come to mind. The actual gross concrement formation of stone would seem to be one of these variants in calcifying pyelonephritis. The accompanying pyelonephritis, tubular and glomerular degeneration, fatty changes, the deposition of urine salts more marked at the site of the stone formation but present in diminishing amount as we proceed to areas away from the stone site, present a histologic sequence that stands strongly for the concept that parenchymal inflammation with secondary crystalline deposition in tissue constitutes a well defined picture of stone formation in infection.

It may be asked why stone formation occurs only at the surface of the pyramid if calcification is present within the renal substance above. The answer is not certain but I would venture the explanation that the intraparenchymal calcium deposits are in contact with only a small amount of urinary fluid as it is being excreted. Furthermore, such intraparenchymal deposits become quickly surrounded by an area of fibrosis which protects them from further deposition of crystalline matter. At the pelvic surface the embryonic stone projects into the renal pelvis. It is constantly bathed by supersaturated urine and fresh deposits occur upon it. This is consistent with what happens in the chemical laboratory when a crystal is suspended in any supersaturated solution. Electrochemical surface reactions occur between the crystalline matter and the colloids and crystalloid ions in solution. Such forces cause a further deposition of colloids and crystalline matter on the surface of the suspended crystal and give rise to further increase in size to the concrement. It is at the site of the papillary crystallinized epithelium that the stone begins. At this site it is exposed to the supersaturated urinary stream and thus invites further crystalline deposition with consequent growth to stone.

URETERAL AND BLADDER STONES

The experimental production of isolated and independent calculosis in the ureter has not as yet been achieved in animals. Nor is there specific evidence that stone ever has its primary genesis in the ureter in the human being. Theoretically this might occur if a localized area of ureteritis should become the site of crystalline deposition. Being continuously bathed in a urine rapidly precipitating its crystalline salts, stone growth could occur. Stones in ureteral diverticula do occur and perhaps their origin may be explained by their formation in degenerative epithelium at these sites.

As for the bladder, experimental and clinical evidence leads us to believe that certain types of cystitis, especially those associated with vesical neck obstruction or with diverticula may be the initiating lesion of stone formation. The stone starts experimentally at least with crystalline deposition on necrobiotic surface epithelium. Now in the bladder we have repeatedly tried to bring about calculus formation by infection with urea-splitting organisms and with mild hyperexcretory states by experimentally producing concomitant vesical neck obstruction. This is done by tying off the urethra of rabbits for 48 hours after the injection of proteus culture or by partly constricting the vesical neck with rubber bands. Such efforts fail utterly unless sharp and distinct chemical or physical trauma has been previously produced, a trauma which destroys to some extent the vesical surface epithelium. From such experiments we must conclude until some controverting evidence is brought forth that bladder stones will arise only from crystalline impregnation of dying surface epithelium. The presence of stasis as always in lithiasis will not initiate the process but will augment its development once calculus formation has begun.

URINARY SEDIMENTS IN STONE-FORMING KIDNEYS

The study of sediments or other material passed in the urine of certain patients with rapidly recurrent showers of calculi or rapidly recurrent stones demonstrated by x-ray, supports to some degree colloid-crystalloid deposition in nephritic tissue as the mechanism of concrement formation. Uratic crystals of fusing

polymorphic types, oxalurias with change of crystal form from octahedral and dumb-bell shapes to fusing spheroidal clusters, polymorphic crystal-colloid aggregates of ammonium magnesium phosphate, and calcium phosphate and the amorphous crystals of calcium carbonate and phosphate have been noted.

We can only conjecture why many of these uraturias, phosphaturias, and oxalurias do not develop stone. Possibly the nephritic element which may change the colloid content of the urine in the tubular pyramids is absent. Only a small percentage of cystinurias develop stone. Hyperthyroidism presents excessive hypercalcinuria, while hyperparathyroidism with its more frequently demonstrable nephritis produces calculi in about 5 per cent of the cases. The same explanation is hypotheticated.

A patient of mine with extensive bilateral urea-splitting proteus infection passed showers of calculi for 16 years. His urine at times was loaded with crystalline-impregnated aggregates of gross form which were found on microscopic study to be composed of a gel-like mucoid substance and degenerated epithelial cells saturated with calcium carbonate crystals in all degrees of density. At death from progressive pyelonephritis, calculosis, and uremia, both kidneys were found to be the seat of multiple calculi and calcific deposition throughout the parenchyma was noted. Microscopically the calculous material attached to the pelvis showed an almost identical morphology with that of the epithelial-crystalloid-colloid aggregates which had been passed in the urine. Both pelves were filled with gritty calcific muco-epithelial tissue surrounding the stones, and all degrees of density from soft pultaceous matter to hard concretions were noted in this material. The renal parenchymal pathology showed diffuse lipomatosis and every degree of calcium impregnation in the tissue. This is the picture of the ultimate degree of calcifying pyelonephritis. (*Figs. 10* and *11.*)

From this background I present the thesis that urinary stone is a phase of calcification or crystalline deposition in necrobiotic tissue. Both the type of nephritic, ureteral, or bladder epithelial degeneration are probably specific for the purpose. On such degenerative lesions crystalline deposition can occur from crystalline hyperexcretion or from bacterial action of type specific and probably most often urea-splitting organisms. Such a thesis does not contradict Randall's concepts of the calcium plaque or of tubular crystalline inspissation. Rather it amplifies and extends these concepts. The nephritic lesions which precede stone may be produced by parathormone as in hyperparathyroid disease, perhaps by vitamin A deficiency, by lipoid changes the result of metabolic change, by bacterial toxins or perhaps by vascular changes

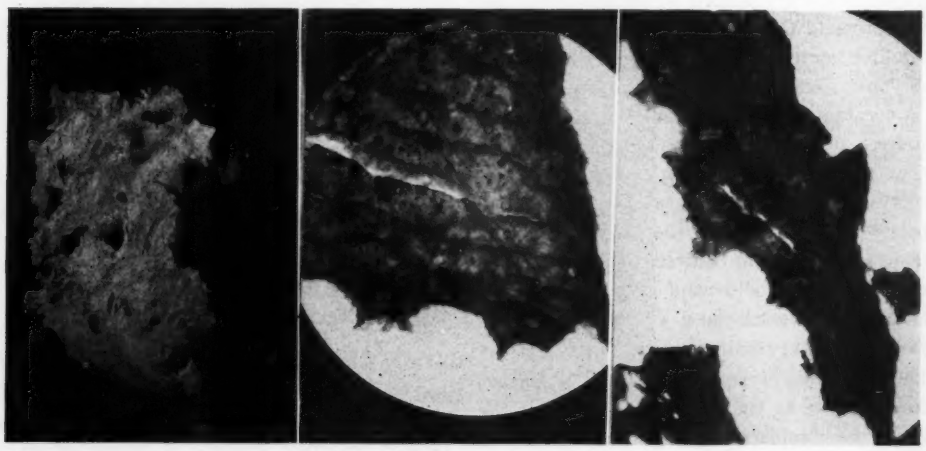

Fig. 10

Gross and microscopic illustration of sheets of degenerated and partly calcified epithelium passed in large quantity in the urine of a patient with bilateral B. proteus infection. This patient had passed hundreds of alkaline stones over a period of 16 years. (Von Kossa stain). At autopsy both kidneys were found filled with pultaceous stones, many attached to the renal pelvic parenchyma. These stones showed a sequential histogenesis from these calcified crystalloid-epithelial aggregates to definite concrements.

with consequent local ischemia, working separately or together. Such a concept is consistent with what we know of the pathologic laws of calcification. Placing this concept alongside the known physico-chemical features of crystalloid-colloid precipitation of water-insoluble matter in urine at different hydrogen-ion range, we can understand the variable composition and the polymorphism that stone disease assumes. In short, the site of stone deposition is at areas of calcium impregnated papillary tissue which is exposed to the urinary stream.

CLINICAL EVALUATION OF THIS CONCEPT OF STONE FORMATION

Is such a concept of calculosis of purely academic value? I think not. From it we come to understand more clearly the pleomorphism of stone, the variability in its site. How aseptic localized nephritis from toxins, from bacterial infection, from nephrotoxic poisons or from ischemia, may provide the superficial epithelial degenerative change which can give rise to stone, becomes clear. The factors of saturation, hydrogen-ion concentration and chemical composition of the urine interplay in the rapidity of stone growth and have to do with its macroscopic form and its chemical composition. We have discussed these factors in many publications and will not recount their individual actions now. With such a background the recurrence of calculus at a given site is better understood.

Also such a picture of stone formation makes us better able to evaluate the measures now common practice in prophylaxis against stone recurrence. Removal of all calculi, cleaning up infection, establishment of better drainage, heminephrectomy or even calyceal resection at times, the correction of hyperexcretory states, the use of vitamins to improve epithelial restoration to normalcy, all are afforded a better scientific background. The limitations of our present efforts at stone dissolution are now clear. The whole picture of calculus formation through the several mechanisms of hyperexcretion, infection and bacterial toxic factors assumes a new aspect.

SUMMARY

In summary, I have reviewed in its simplest aspects the evidence now at hand from experimental, clinical and pathologic studies into the cause of urinary calculi. I have proposed and supported the thesis that instead of arising from crystalline deposition from the free urinary stream after excretion, stone arises from a precedent lesion in the surface epithelium of the

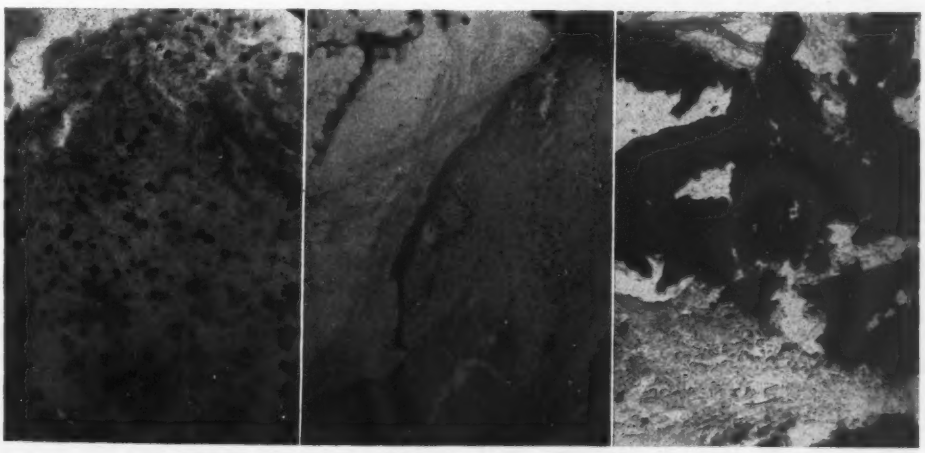

Fig. 11

Areas of renal parenchyma in patient whose urinary sediments are depicted in *Fig. 10.* (Von Kossa stain). (*Left*) Area somewhat distant from surface. (*Center and right*) Hyalinized and degenerated surface epithelium with progressive massive calcification at surface leading to stone growth from this surface into the calices.

urinary tract with subsequent deposition of crystalline matter at the site of this lesion. An attempt has been made to show how the various mechanisms of stone formation assume their respective activities on such a pathologic basis.

Admittedly there are many gaps in our knowledge as to the cause of such localizing lesions in the urinary epithelium and our concepts of the various mechanisms producing a stone forming urinary tract are all too inadequate. Nevertheless as we take stock of the evidence which we have, the result of research for the past twenty-five years, we must come to think of stone formation in a new light. It is a pathologic process involving localized injury to the surface epithelium of the urinary tract by metabolic, toxic or bacterial agency with the subsequent deposition of crystalline matter when and where such sites are exposed to a supersaturated urinary stream capable of concomitantly precipitating crystalline and colloid material thereon.

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BIBLIOGRAPHY

1. Grossman, W.: Beitrage zur Pathologic und Klinik der Harnsteinkrankheit Zeitschift f. Urolog. Chirurgie, **35**:78, 1932.
   Untersuchungen uber Nierensteinen. Zeitschift f. Urolog. Chirurgie, **38**:264, 1933.
2. McCarrison, R.: The Experimental Production of Stone in the Bladder. Brit. Med. Jour., **1**:717, 1927.
   The Experimental Production of Stone in the Bladder of Rats. Brit. Med. Jour., **2**:717, 1927.
3. Randall, A.: Hypothesis for Origin of Renal Calculus. New. Eng. J. Med., **214**:234, 1936.
   Initiating Lesions of Renal Calculus. Surg. Gynec. & Obst., **64**:201, 1937.; Trans. Am. Assoc. G. U. Surg., **20**:323, 1936.
   A Hypothesis for the Origin of Renal Calculus. J. New Eng. Branch, A.U.A., **3**:6, 1936.
   The Origin and Growth of Renal Calculi. Ann. Surg., 1937, 1009.
   Papillary Pathology as a Precursor of Primary Renal Calculus. J. Urol., **44**:580, 1940.
   The Etiology of Primary Renal Calculus. Int. Abst. Surg., **71**:209, 1940.
   And Eiman, J. E.; and Lebermann, P. R.: Studies on the Pathology of the Renal Papilla. J.A.M.A., **109**:1690, 1937.
   And Campbell, E. W.: Alkaline Encrusted Cystitis. J. Urol., 1937, **37**:264.
   And Melvin, P. D.: The Morphogeny of Renal Calculus. J. Urol., **37**:737, 1937.
4. Hench, P. S.: Diagnosis and Treatment of Gout and Gouty Arthritis. J.A.M.A., **116**:453, 1941.
5. Hegar, B. H.; and Magath, T. B.: The Etiology of Encrusted Cystitis with Alkaline Urine. J.A.M.A., **85**:1352, 1925.
   The Formation of Vesical Calculi. J.A.M.A., **90**:266, 1928.
6. Davalos, A.: Experimental Production of Stones in the Bladder. J. Urol., **49**:639, 1943.
7. Hellstrom, J.: Einige Ehrfahrungen ueber Entstehung, Wachstum, und Spontanen Abgang von Neirensteinen. Zts. f. Urol. Chir., **18**:248, 1925.
   The Significance of Staphylococci in the Development and Treatment of Renal and Ureteral Stones. Brit. Med. Jour., **10**:348, 1938.
8. Hryntshak, T.: Experimentelle Untersuchungen zur Harnsteinentstehung. Zts. f. Urol. Chir., **40**:15, 1935.
9. Posey, L.: Urinary Concretions. J. Urol., **48**:300, 1942.
10. Higgins, C. C.: Experimental and Clinical Observations on Urinary Calculi. New Eng. J. Med., **214**:1007, 1935.
    Prevention of Recurrent Calculi. Surg. Gynec. & Obst., **63**:23, 1936.
    Present Status of Dietary Regimen in the Treatment of Urinary Calculi. Brit. J. Urol., **9**:36, 1937.
    Urinary Lithiasis: Experimental Production and Solution with Chemical Application of End Results. J. Urol., **36**: 128, 1938.
    Factors in Recurrence of Renal Calculi. J.A.M.A., **113**: 1460, 1939.
    Urinary Lithiasis: Collective Review. Int. Abst. Surg., **68**:392, 1939.
    The Management of Ureteral Calculi. Am. Surg., **115**:369, 1942.
    And Mendenhall, E. E.: Factors Associated with Recurrent Formation of Renal Lithiasis with a New Method for Qualitative Analysis of Urinary Calculi. J. Urol., **42**:436, 1939.
11. Keyser, L. D.: The Mechanism of the Formation of Urinary Calculi. Ann. Surg., **77**:210, 1923.
    The Etiology of Urinary Lithiasis. Arch. Surg., **6**:525, 1923.
    Urinary Lithiasis: Its Cause and Prevention. South. Med. Jour., **25**:1031, 1932.
    The Relationship of Urinary Infections to Recurrent Calculi. J. Urol., **31**:219, 1934.
    Recurrent Urolithiasis: Etiologic Factors and Clinical Management. J.A.M.A., **104**:1299, 1935.
    Urolithiasis: A Clinical and Experimental Study. Address Genito-Urinary Section, N. Y. Acad. Med., Oct. 1934. (Unpublished.)
    Stone in the Urinary Tract: Present Concepts of Etiology and Preventive Therapy Against Recurrence. Address Philadelphia Urol. Soc., Oct. 1936. (Unpublished.)
    Calculous Disease in the Urinary Tract. Address Nov. 1937, N. Y. Post-Grad Fortnight, Bull. N. Y. Academy of Medicine, **14**:76-92, 1938.
    Stone in the Urinary Tract. Virg. Med. Monthly, April 1937.
    Newer Concepts of Stone in the Urinary Tract. J. Urol., **42**:420, 1939.
    Urinary Lithiasis: Review of a Quarter Century of Research. J. Urol., **50**:169, 1943.
    Studies in Urinary Calculosis. Address before N. Y. Society of the A. U. A., 1944. J. Urol. (in press.)

DISCUSSION (*Abstract*)

Dr. Wm. M. Coppridge, Durham, N. C.—Dr. Keyser's work is a fine example of what a busy clinical man can do in the way of scientific research if he has the ability and energy. He has created his own opportunity for research.

I can certainly add nothing to what he has told us concerning the genesis of stone. Those of us whose work and experience has been entirely on the clinical side of the subject do over the years gain certain impressions of the problem that may or may not be of value when passed on to others. There are a few points of this kind that I would like to make.

(1) We must keep constantly in mind the fact that primary stone formation is the real problem. Other factors that lead to secondary stone formation have little or nothing to do with the genesis of the disease. Such factors as retention, vitamin deficiency, or lower urinary tract infection, which may promote the growth of stone after the nidus or nucleus is formed are only secondary factors and probably have little to do with the beginning of stone.

(2) I am glad to note that Dr. Keyser's work has fur-

ther supported that of Randall and others that primary stone arises from a pathological lesion on the surface epithelium of the urinary tract. Gross examination of practically all small primary stones shows an area of roughening which is undoubtedly the point of former attachment to the diseased mucous membrane.

(3) It seems logical, though not entirely proven perhaps, that bacterial action either toxic or infectious, produces the necrosis and calcium deposition which provides the original nidus.

(4) We have for years done routine urine cultures in ureteral stone cases. Making adequate allowance for the error of contamination we have found that the majority of the primary stone cases show staphylococci on urine culture. In our experience, urea splitting organisms are almost never found in primary stone cases; they are frequent in secondary stones that have had surgery or repeated instrumentation. From purely clinical study over the years we have the definite feeling that staphylococci or their toxins are a preponderant factor in primary stone formation. Randall did not find incidence of infection around the calcium plaques but Rosenow and others have reported finding staphylococci.

We have felt that the high natural resistance to staphylococci and other pyogenic organisms that is known to exist in certain races, particularly the Negro, may explain the low incidence of stone in these races.

There is certainly little clinical evidence that vitamin A deficiency is a factor in stone formation in the human. Of considerable interest is a series of cases published a few years ago, of cystic pancreatitis in children. In this disease the child is unable to use any vitamin A because of the complete lack of pancreatic secretion. In this series of over 50 cases, children who had lived from a few months to several years, with no vitamin A, on post mortem examination only one child showed any evidence of pathology of any extent in the urinary tract. In this case one small stone was found in the kidney.

It would seem that in this problem, animal experimentation has been less productive of convincing results than studies conducted upon the human kidney.

Clinically, stasis plays no role in primary stone formation. Very few cases of early small stone show any degree of hydronephrosis, while on the other hand congenital hydronephroses from uretero-pelvic obstruction attain massive proportions, usually without stones being formed.

This is undoubtedly urology's number one problem. Stone's prevalence and devastating effect on human health and happiness should continue to give us much concern.

Dr. R. H. Flocks, Iowa City, Iowa.—Dr. Keyser has done more work on urinary lithiasis than anyone in this country, and I have followed it with very great interest. His presentation was quite convincing, and I am sure that at least a great proportion of the stones that we see, come about in the manner that he has shown.

We should realize that they do come about that way, because it may change our indications with regard to conservative or more radical therapy in individual patients. For example, in a patient who has a perfectly good kidney on one side, and a fairly large stone on the other, or possibly two or three stones, one may consider a nephrectomy rather than simply removing the stone, if he realizes that possibly a great deal of kidney tissue is permeated with these lesions which Dr. Keyser has demonstrated to us.

However, there are some cases, especially cases associated with fractures of the femur or of the spine, in which no infection is present, where these kidney lesions are not present, and there has been an actual precipitation of calcium particles around the calices. Some cases which I have seen like that with large numbers of tiny calculi right about the calices wash out very easily, and then the whole process clears up. In some of those cases we have had opportunity to examine the kidneys and the kidneys have not shown anything microscopically. In a group of 52 kidneys that we studied several years ago, all of which had had stones, only about 75 per cent showed lesions microscopically and therefore I do believe there are some cases where the actual precipitation takes place in the lumen of the urinary tract.

I agree with Dr. Keyser that in at least many of the cases, possibly the majority of them, these nephritic lesions occur. In some cases they may be secondary to the stones in the lumen but in either case they must be considered in the care of the patient and the care of that particular kidney.

Dr. Keyser (closing.)—I have been somewhat adventurous in putting down this material positively. In the manuscript some qualifications are made. For years I did think that especially in hyperexcretory states, clusters of crystals might hide in calyceal pockets. Then they might become somewhat compacted or condensed and ultimately become the nucleus of stones. This may still be so in certain instances but I believe they are rare. However, we see a great many stone-bearing kidneys that do not manifest in any demonstrable degree these calcific changes which I have described. Nevertheless, the lesions associated with stone formation may be very small, perhaps very transient. They must of necessity be sometimes capable of healing, and epithelial restoration to normality with good function must usually take place. Stones once removed do not always recur.

I have tried to bring to your mind the thesis that stone "grows out of the kidney" rather than that "stone is deposited in this organ." Whether this concept will be retained over the years, whether I may be compelled to change my views, are open questions. We must keep an open mind on this of all subjects in urology. I hope that I have given you, if nothing else, food for thought.

GENERAL MANIFESTATIONS OF SALICYLISM*

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and
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Although salicylates have been used in the treatment of rheumatic fever and for relief of pain in the other arthritides, for nearly seventy years, not until the recent work of Coburn[1] has it become customary to administer massive doses of salicylates over a protracted interval. Little attention has been directed towards the possible toxic effect of the drug when used over a long period with high plasma levels and high tissue saturation. Coburn[1] has said that the only toxic symptom ordinarily observed was a "mild tinnitus"; however, one case developed alarming symptoms of intoxication characterized by fever, a cutaneous eruption and psychosis. He stresses the importance of continuing a high plasma level over a period of several weeks, advocating the administration of the drug even after all clinical manifestations of the illness have subsided. He recommended ten grams of salicylate daily, to be given intravenously until the sedimentation rate falls 20 per cent, then the oral administration of ten grams per day, giving 1.66 grams every four hours. He feels that blood levels of 360 gammas per c.c. should be promptly reached and retained for some weeks. It is our belief that the intravenous route is unnecessary, and satisfactory and more constant levels are more easily maintained by the oral method.

In the application of this therapeutic procedure in a comparatively small series of cases, we have encountered troublesome and potentially serious toxic reactions and the purpose of this paper is to emphasize the importance of recognition of these untoward symptoms and to suggest a therapeutic regime for their control.

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Thirty-Eighth Annual Meeting, St. Louis, Missouri, November 13-16, 1944.

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The active principle of all the salicylates is salicylic acid and the analgesic and antipyretic effect of salicylates, long recognized, is thought to be due to the effect of salicylic acid on the hypothalamus, causing reduction of fever and obtundation of pain. According to Lutwak-Mann, they exert a profound effect on carbohydrate metabolism, causing complete disappearance of liver glycogen in some cases. The central action of the drug is probably also responsible for most of the toxic phenomena associated with its use. The most commonly seen unfavorable reactions are tinnitus, dizziness, nausea, and vomiting, while fever, tachypnea, cutaneous eruption, mental unrest and coma are not rare.

(1) *Tinnitus.*—It is well known that the auditory nerve is more affected than any other nerve of special senses by the action of salicylates circulating in the blood, just as is true in quinine. The drug frequently causes subjective noises and deafness of a varying degree, which is usually temporary, when it is used in large doses or over a long period. The deafness is caused by the toxic action on the ganglia cells of the cochlea and their associated nerve fibers and there have been demonstrated changes in the endothelial lining of the small capillaries and vasoconstriction with resulting ischemia and anoxemia.

Taylor[2] emphasized the fact that the deafness often attributed to toxemia of rheumatic fever may be due to the salicylate administered the patient. Loberg[3] in 1926 found sodium salicylate in the cerebrospinal fluid of normal persons receiving six grams per day, as did Beruard and Daniel[4] in 1933. This suggests that the drug passes through the stria vascularis into the endolymph or that the drug in the spinal fluid passes up the aquaeductus cochlea.

(2) *Dizziness.*—In our experience, this is the second most commonly encountered untoward subjective complaint. It consists of unsteadiness which is not a true vertigo but an annoying disturbance of equilibrium.

(3) *Nausea and Vomiting.*—For years it has been taught and accepted that the nausea and vomiting associated with salicylate therapy have been caused by the local action of the drug on the gastric mucosa, so that it has been an accepted custom to prescribe sodium bicarbonate

in appropriate dosage, in conjunction with the oral administration of salicylates. Schnedorf, Bradley and Ivy[5] have said that sodium bicarbonate is helpful because it protects against the release of salicylic acid. In the series of cases that we have treated with massive salicylate therapy, we have observed that patients receiving the drug intravenously have experienced the same or even more nausea and vomiting than those who receive it orally, and it has been further observed that in patients receiving salicylates, the oral administration of sodium bicarbonate will produce symtomatic relief from intractable nausea.

Smull[6] and her co-workers have recently shown that the administration of sodium bicarbonate will promptly and materially reduce the plasma salicylate level and that the simultaneous administration of the two drugs will prevent the attaining of a satisfactory high level. This, we have observed beyond reasonable doubt and believe that it is due to an increased urinary excretion of salicylates, with consequent fall of circulating salicyl radical and a prompt lessening of its central action.

We have conducted some studies to ascertain gastric secretory and mucosal changes during massive salicylate therapy. While the plasma level was at maximum height during intravenous administration of salicylates, aspirations of gastric juice were performed and analyses made for salicylates. In no case were we able to demonstrate even a trace of salicylate in the gastric secretion. Further, there has been no significant increase or reduction in titrable acidity in any of our cases. Gastroscopic examinations were performed on three of our patients suffering with nausea, while receiving oral salicylates in large doses. In none of these was any abnormality of the mucosa or any other significant pathological finding noted on endoscopic examination.

Hurst and Lintott[7] in 1939 called attention to the fact that hematemesis may occur after the administration of a single dose of aspirin. We think that this probably represents an individual idiosyncracy or an anaphylactic reaction to the drug and that this same reaction does not occur in normal individuals receiving salicylates.[8 9 10] Acetylsalicylic acid is the most common salicylate compound causing allergic phenomena. These reactions are due to unexplained hypersensitivity and may occur, as stated above, after the ingestion of a small amount of the drug. Paul,[11] in his study of 228 cases before and after the oral administration of aspirin, concluded that aspirin did not produce hyperemia or hemorrhages in the gastric mucosa in any case studied by him.

From the above studies, it appears evident that the nausea and vomiting experienced by patients receiving salicylates in any form is probably due to the central action of the drug on the higher cerebral centers and not often to the local action on the mucosa of the gastrointestinal tract.

(4) *Hyperpnea.*—There is a type of respira-

GAMMA PER C.C.

Name	DRUG (10 GM)	TOXIC SYMPTOMS N	V	T	D	MISC.
A.N.	I.V. SODIUM SALICYLATE	0	++	0	++	CHILL FEVER
R.W.	I.V. SODIUM SALICYLATE	0	0	++	++	0
H.S.	I.V. SODIUM SALICYLATE	++	0	++	0	0
C.C.	ORAL SODIUM SALICYLATE	0	0	+	0	0
W.B.	ORAL SODIUM SALICYLATE	+	0	++	+	0
L.S.	ORAL SODIUM SALICYLATE	++	0	++	+	0
J.S.	ORAL ACETYL-SALICYLIC ACID	++	0	++	+	DYS
J.G.	ORAL ACETYL SALICYLIC ACID	0	0	++	0	0
T.S.	ORAL ACETYL SALICYLIC ACID	++	0	++	+	0

N=Nausea V=Vomiting T=Tinnitus D=Dizziness

Graph 1

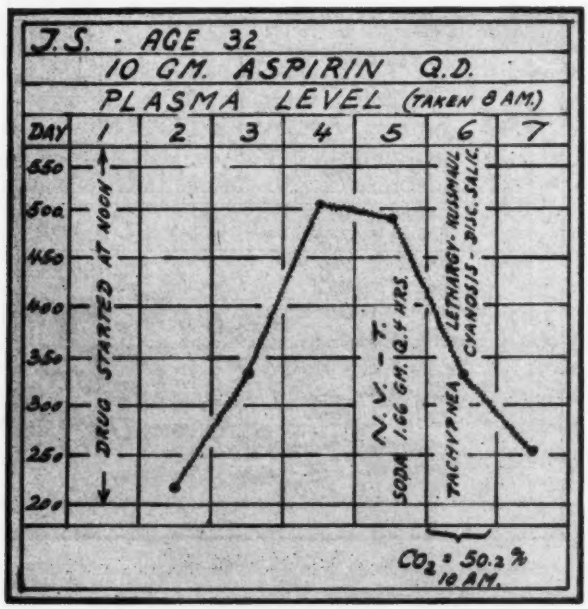
Toxic reaction during salicylate therapy.

Patient No. 1 was the only case experiencing vomiting and was receiving intravenous salicylates.

tory involvement known as "salicyl dyspnea" which resembles closely Kussmaul's breathing, that is often seen in advanced stages of salicylic intoxication. This hyperpnea is thought to be due to the effect of the salicyl radical on the respiratory center in the medulla. We have seen this interesting phenomenon in our series and were impressed with the similarity between it and that type of pathological breathing seen in acidotic coma. However, there was no evidence of a disturbance of the acid base equilibrium in the circulating blood, the carbon dioxide combining power being 50.2 volumes per cent. Dodd, Minot and Arena[12] demonstrated in dogs, toxic from salicylates, essentially normal acid base equilibrium in the blood during normal respiration, but in peripheral blood aspirated after the animal experienced tachypnea, a low-grade alkalosis, with increased pH, developed. This was probably due to loss of carbon dioxide in the expired air, with compensatory decrease in alkali reserve of the blood. Acidosis has been reported,[13] but analysis of case reports indicates it occurs only after marked dehydration as a result of increased heat and fluid loss, with hemoconcentration and consequent inadequate circulation, which cannot meet the demands for oxygen and for removal of carbon dioxide. It appears likely then, that the tachypnea, characteristic of the toxic action of salicylic acid, is caused by its direct effect on the respiratory center, stimulating respiration just as ketone bodies do, as has been emphasized by Odin,[14] and discussed by Bowen,[15] Quincke,[16] and others.

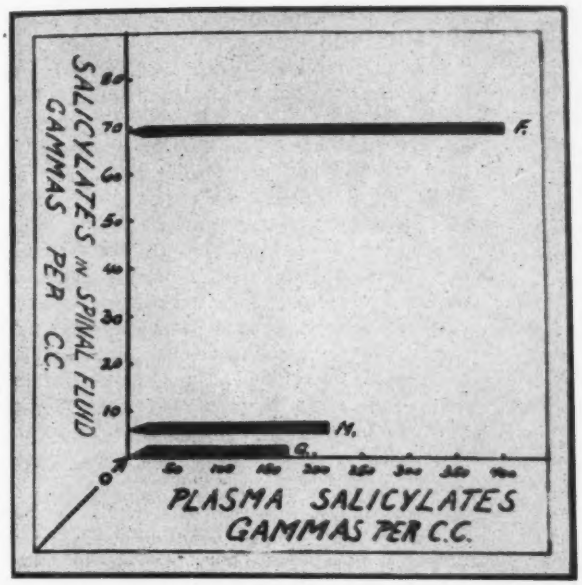
Coombs, Warren and Higley[17] have recently corroborated the above, saying that the accumulation of salicylates in the blood leads to direct stimulation of the respiratory center and thus to hyperventilation alkalosis. They showed early changes in the blood, with slight rise in pH and lowering of CO_2 content and agreed that this was probably due to a compensatory alkalosis.

(5) *Mental Symptoms.* — Mental excitation, dullness, lethargy, confusion, delirium, coma or even death, have been reported as due to toxicity of salicylates. Central excitation may be prominent and this abnormality has been referred to as the "salicyl jag" and it is characterized by restlessness, incoherent speech, occasionally mania and hallucinations. As poisoning progresses, central stimulation is replaced by increasing depression, with lethargy, stupor and coma. The threshold of tolerance for each individual appears to be different but if high plasma levels, that is, above 360 gammas per c.c. are retained over a long period of time as suggested by Coburn,[1] a fair percentage of all patients will develop some significant mental symptoms. Dialysis of salicylates through the meninges[18] occurs after high plasma levels are reached. The following chart will demonstrate the meningeal threshold for salicylic acid. It will be noted that small amounts of the drug are found in the spinal fluid after a plasma level of 200 gammas per c.c. is reached and it will increase as the blood concentration rises.



Graph 2
Hyperpnea and semi-coma occurring during massive salicylate therapy.

Link[19] and others have shown that salicylic acid may cause temporary prolongation of the prothrombin time



Graph 3
Meningeal threshold for salicylates.

in animals and this has been reported in humans. In our small series of cases we have encountered hypoprothrombinemia in one case, the level going to 70 per cent of the normal. If larger series are studied, this finding may be more frequent and, if so, its importance should be stressed as serious hemorrhage may result. We have found no reported cases of massive cerebral hemorrhage during salicylate therapy but on autopsies of animals who have received salicylates over a long period of time, small petechial hemorrhages have been described throughout the entire cerebrum.

Failure to recognize the occurrence of severe toxic mental changes leads to profound coma and ultimate death. When these symptoms are noted, appropriate treatment should be promptly instituted and should consist of the following:

(1) Discontinue the drug.

(2) Give large doses of sodium bicarbonate; this will cause diuresis, raise the pH of the urine and promptly reduce the plasma salicylate level.

(3) Establish proper hydration with adequate fluids, either orally or parenterally.

(4) Apply cooling measures for fever, if present.

(5) Give food to meet excessive catabolism.

(6) If central depression is marked, caffein or ephedrine may be required.

CONCLUSIONS

(1) Evidence has been presented that indicates that the prominent symptoms of salicylism are manifestations of the central effect of the drug; that tinnitus, dizziness, nausea, vomiting, fever, tachypnea and encephalopathies noted when large doses of salicylates are administered are caused by the effect of the drug on the higher centers.

(2) That intravenous salicylate therapy is unnecessary.

(3) That alkalies should not be given concomitantly with salicylates when it is desirable to reach a high plasma level, but should be reserved for use when toxic symptoms develop.

(4) That plasma salicylate levels are promptly reduced by alkali therapy.

(5) That an awareness of the toxicity of salicylates should be constantly present when administering the drug in large doses or over a prolonged period.

BIBLIOGRAPHY

1. Coburn, A. F.: Salicylate Therapy in Rheumatic Fever, A Rational Technique. Bull. Johns Hopkins Hosp., **73**:435-464, 1943.
2. Taylor, H. Marshall: Medicine of the Ear. Fowler, 340, 1939.
3. Loberg, K.: Eine klinische Methode zur quantitativen Bestimmung von Salicylsaure im Blutserum und Liquor cerebrospinalis. Biochem. Ztschr., **170**:173, 1926.
4. Beruard, G.; and Daniel, M.: Rapports du salicylate de sodium et de l'iodure de sodium dans le sang et dans le liquide cephalorachidien. Compt. rend. Soc. de biol., **112**: 176, 1933.
5. Schnedorf, J. G.; Bradley, W. B.; and Ivy, A. C.: Effect of Acetylsalicylic Acid upon Gastric Activity and the Modifying Action of Calcium Gluconate and Sodium Bicarbonate. Amer. J. Digestive Dis., **3**:239-244, 1936.
6. Smull, Katharine; Wegria, Rene; and Leland, Jessica: Effect of Sodium Bicarbonate on Serum Salicylate Level During Salicylate Therapy of Patients with Acute Rheumatic Fever. J.A.M.A., **125**:1173 (Aug. 26) 1944.
7. Hurst, A.; and Lintott, G. A. M.: Aspirin Haematemesis: Clinical and Gastroscopic Study. Guy's Hosp. Rep., **89**:173-183, 1939.
8. Prickman, L. E.; and Buchstein, H. F.: Hypersensitivity to Acetylsalicylic Acid. J.A.M.A., **108**:445-451, 1937.
9. Hitch, F. G.: Fatal Case of Poisoning by Aspirin. J. Roy. Nav. M. Serv., **19**:295 (Oct.) 1928.
10. Dyke, S. C.: A Case of Acetylsalicylic Acid Poisoning. Lancet, **2**:613 (Sept. 14) 1935.

11. Paul, Wm. D.: The Effect of Aspirin on the Gastric Mucosa. J. Iowa M. Soc., **33**:155-158 (April) 1943.
12. Dodd, Katharine; Minot, Ann S.; and Arena, Jay M.: Salicylate Poisoning: An Explanation of the More Serious Manifestations. Am. J. of Dis. of Child., **53**:1435-1446, 1937.
13. Johnson, C. C.: The Salicylates. XIX. The Question of Acidosis Following the Administration of Salicylates. J.A.M.A., **94**:794 (March 15) 1930.
14. Odin, M.: Is Salicyl Poisoning an "Acidosis"? Acta. Med. Scandinav. (supp.), **50**:177, 1932.
15. Bowen, B. D.; Ronfa, J. F.; and Clinger, O. W.: Diff. Diagnosis of Salicylate Poisoning and Diabetic Acidosis., J.A.M.A., **107**:276 (July 25) 1936.
16. Quincke, H.: Zur Keuntuis der Salicyclsaurewirkung. Berl. Klin. Wclinsthr., **19**:709, 1882.
17. Coombs, F. S.; Warren, H. A.; and Higley, C. S.: Unpublished data. Paper presented before Central Society for Clinical Research (Nov. 4) 1944.
18. Livon, Charles; and Bernard, J.: Cited in Johns Hopkins Press, 1935, page 302, The Cerebrospinal Fluid and Its Relation to the Blood.
19. Link, et al.: J. Biolog. Chem. (Feb.) 1943.

ACUTE BARBITURATE POISONING

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INTRODUCTION

The purpose of this paper is to present the signs, symptoms and treatment of 49 cases of acute barbiturate poisoning seen at Charity Hospital, New Orleans, from 1938 to 1943 inclusive. In recent years there has been extended use of various malonylurea derivatives as sedatives by both physicians and laymen, and accordingly a marked increase in accidental and suicidal intoxication. Since not all states require a prescription for dispensation of the barbiturate group of drugs they can be easily obtained by the laiety. In those states where a physician's order is required, each prescription should have "Do Not Refill" written upon it.

It is essential that all physicians consider the possibility of acute barbiturate poisoning in any patient admitted to the hospital in coma since without a history of ingestion of barbiturates the diagnosis is rarely self-evident and is made only after exclusion of the numerous other causes of coma, such as diabetic coma, uremia, cerebro-vascular accidents, head injuries, virus infection of the central nervous system, alcoholism, and so on.

Usually the patient is comatose, but may exhibit marked psychomotor stimulation. The pupils are contracted or dilated with a sluggish or absent accommodation to light. The respirations may be slow and shallow, or rapid and shallow, and cyanosis is not uncommon. The reflexes are usually sluggish or absent. The blood pressure is generally lowered and the pulse rapid and thready. Death occurs following respiratory arrest, circulatory collapse or at a later date from bronchopneumonia or other pulmonary complications. Diagnosis may be aided by recovery of colored gelatin capsules in the return from a gastric lavage. The fatal dose of the barbiturates is generally 15 to 30 times the therapeutic dose of the given preparation.[1]

RESULTS AT CHARITY HOSPITAL

Table 1 gives the pertinent data concerning the forty-nine admissions. Twenty-one were males (one being admitted four times) and twenty-five were females; of this number forty-one were white and five colored. Of the drugs taken, twenty-four were unknown; seven patients took "amytal," six phenobarbital, four barbital, two "seconal," two "veronal," and one "nembutal." Combination of drugs taken were: "seconal," "nembutal," phenobarbital and one grain of codeine; "amytal," bromide, aspirin and two grains of morphine; and "barbiturate and several strychnine tablets."

The mental state varied from one of confusion to coma of four days' duration. In those cases where blood pressure was recorded, only five were found to have a systolic pressure of 100 or below. Respirations on admission varied from eight to sixty-four per minute; of this number seven were sixteen per minute or below and two above thirty per minute; three were not recorded. The temperature ranged from 98 to 99° in thirty-three cases, below 98° in three, above 99° in eleven, and was not recorded in two. The condition of the pupils was normal in twenty-three, not described in fourteen, constricted in seven and dilated in five. The reflexes were normal in twenty-three cases, not stated in eight, hypoactive in seven, hyperactive in six, and absent in five. Two patients showed an erythematous maculo-papular rash. Emesis

*Received for publication May 19, 1945.

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occurred only once. Concerning the personality make-up of the patients, seven had previously been seen in the hospital and diagnosed as psychoneurotics.

Five or 9.8 per cent of the admissions were fatal. Of this number, one died of respiratory arrest. In this case, admission was 1½ hours after ingestion of "several capsules and tablets of 'seconal,' 'nembutal,' phenobarbital and one grain of codeine." Death occurred 1½ hours after admission. Therapy included picrotoxin, metrazol, "coramine," oxygen, and the use of a Drinker respirator. Two died of bronchopneumonia; one was admitted 14 hours after ingesting an unknown amount of a barbiturate (verified by blood studies) and died 2½ days later without regaining consciousness. Treatment consisted of caffeine sodium benzoate, metrazol and intravenous glucose. The second patient with pneumonia was admitted 18 hours after ingesting an unknown amount of "a barbiturate" and died 3 days later, remaining comatose the entire time. Therapeutic measures used were picrotoxin, sulfathiazole and intravenous glucose and normal saline. Two patients died in uremia on the day of admission. One, a known drug addict, ingested 150 grains of an unstated barbiturate and died 18 hours later. Therapy consisted of caffeine sodium benzoate, hypertonic glucose, oxygen and temperature measures (the temperature rose from 102° to 106° at death). The second uremic patient was found comatose and until a history was obtained a differential diagnosis of uremia, diabetic coma, cerebro-vascular accident and hysteria was entertained. A coroner's report stated "chemical analysis showed appreciable amounts of barbiturate present" and uremia. Gross changes described were "hemorrhagic bronchitis and cloudy swelling of the kidneys."

Overdosage of barbiturates was intentional (suicidal) in eighteen and accidental in thirteen. Ten were alcoholics or drug addicts and were taking the barbiturate to prolong the effect, or in an effort to break themselves of the drug habit. In eight cases the reasons were not stated.

DISCUSSION

From the above data it can be seen that the diagnosis of acute barbiturate poisoning is not easy in the absence of a history of drug ingestion or when gastric lavage fails to reveal any telltale undigested colored capsules. An early diagnosis is essential if life-saving treatment is to be instituted.

The treatment of acute barbiturate poisoning should employ the following principles: (1) Removal of the drug from the gastro-intestinal tract, (2) administration of drugs to counteract the depressant effect on the central nervous system, (3) prevention and treatment of circulatory collapse, and (4) measures to prevent secondary infection, particularly bronchopneumonia.

(1) Gastric lavage should be done routinely at the first possible moment even if the patient has been in coma for hours, since pylorospasm and retention of the drug are not uncommon. The stomach should be lavaged three separate times with at least one quart of warm water for each washing. After the last lavage, two ounces of magnesium sulfate should be left in the stomach to promote rapid evacuation.

(2) Drugs most effectively used by themselves or in combination include caffeine sodium benzoate, "coramine," strychnine, and picrotoxin. The caffeine salt may be given intramuscularly in the dose of 0.5 gram every hour or two as needed. Enemas containing strong black coffee are also helpful. The main therapeutic use of "coramine" is as a respiratory stimulant. It does not compare in efficiency with strychnine, caffeine or picrotoxin and should not be the drug of choice in combatting combined circulatory and respiratory depression.[2]

Strychnine stimulates respiration, lessens the degree of coma through its action on higher centers, stimulates the medullary vasomotor centers and increases the reflex activity of the spinal cord. Strychnine may be given intramuscularly in doses from 2 to 10 mg. and repeated approximately every two hours depending on the patient's response.[2]

Picrotoxin is apparently the most effective physiological antagonist to the barbiturates.[2] The usual commercial solution of this drug contains 3 mg. per cubic centimeter. Usually the picrotoxin is given intravenously (by injection through the tube of a previously set-up intra-

Patient	Age	Dosage Grains	Drug	On Admission					Reason for Taking
				Blood Pressure	Resp. Per Min.	Temp.	Pupils	Reflexes	
W.M.*	36	10	N.S.	110/160	15	96.2*	N.S.	Hyperactive	Accidental
W.M.	43	N.S.	"Amytal"	138/78	22	101.5	Normal	Normal	Suicidal
W.M.	38	N.S.	"Amytal"	130/80	32	101	Normal	Hypoactive	N.S.
W.M.	29	N.S.	N.S.	115/80	22	99.4	Normal	Hyperactive	Drug Addict
W.F.	32	12	"Amytal"	110/68	20	98	N.S.	N.S.	Suicidal
W.M.	26	N.S.	N.S.	70/50	20	99	Dilated	Hypoactive	Drug Addict
W.M.	26	N.S.	N.S.	120/80	19	97	Normal	Normal	Drug Addict
W.M.	26	N.S.	N.S.	118/80	8	99	Constricted	Hypoactive	Drug Addict
W.M.	26	N.S.	N.S.	N.S.	N.S.	98	Normal	Hypoactive	Drug Addict
C.F.	22	60	Phenobarbital	100/80	24	98	N.S.	Absent	Suicidal
W.F.	24	12	N.S.	110/65	20	99	Constricted	Hypoactive	Drug Addict
W.F.	26	N.S. (plus	N.S. 9/50th Strychnine)	N.S.	28	100	Normal	Hyperactive	Suicidal
W.F.	27	N.S.	N.S.	120/90	23	99	Normal	Normal	Accidental
W.F.	26	9	Phenobarbital	110/70	14	98	Normal	Normal	N.S.
W.F.	23	27	"Amytal"	120/80	20	99	Constricted	Hypoactive	Suicidal
W.F.	19	N.S.	N.S.	120/90	30	100	Constricted	Normal	N.S.
W.M.	70	N.S.	N.S.	N.S.	20	99	Normal	Normal	N.S.
W.F.	29	18	"Seconal"	120/80	20	99	N.S.	Hyperactive	Accidental
W.F.	26	37½	"Veronal"	N.S.	25	99	Dilated	Hypoactive	Suicidal
W.F.	28	9 90 80 2	"Amytal" Bromide Aspirins Morphine	130/70	20	99	Constricted	Normal	Suicidal
W.F.	31	150	N.S.	90/50	64	103	Dilated	Absent	Drug Addict
W.M.	34	N.S.	N.S.	N.S.	20	98	Normal	Normal	Suicidal
C.F.	34	N.S.	N.S.	110/70	25	102	Normal	Normal	N.S.
W.M.	30	N.S.	N.S.	120/85	26	99	Normal	Hyperactive	Suicidal
W.M.	33	36	"Amytal"	108/80	20	100	Dilated	Normal	Accidental
W.M.	28	70	N.S.	N.S.	28	99	Dilated	Normal	Drug Addict
W.M.	41	9	"Amytal"	120/80	25	99	N.S.	N.S.	N.S.
W.M.	36	20	Barbital	112/80	25	98	Normal	Normal	Alcoholic
W.M.	33	26½	"Amytal"	120/70	25	100	Normal	Absent	Suicidal
W.M.	32	N.S.	"Veronal"	140/100	30	100	Normal	Normal	N.S.
W.M.	48	N.S.	Barbital	N.S.	26	98	N.S.	N.S.	N.S.
W.F.	N.S.	N.S.	Barbital	80/50	30	99	N.S.	Absent	Suicidal
W.F.	24	N.S.	N.S.	110/50	25	99	N.S.	N.S.	Accidental
W.F.	18	N.S.	N.S.	N.S.	14	98	N.S.	N.S.	Suicidal
W.F.	15	9	Phenobarbital	110/60	17	97	N.S.	N.S.	Suicidal
W.F.	39	9	Phenobarbital	N.S.	16	98	N.S.	N.S.	Suicidal
C.F.	30	N.S.	N.S.	N.S.	25	103	Normal	Normal	Accidental
W.F.	17	9	"Seconal"	N.S.	25	99	Normal	Normal	Suicidal
W.F.	24	N.S.	N.S.	N.S.	20	98.5	Normal	Normal	Accidental

Table 1

Patient	Age	Dosage Grains	Drug	On Admission: Blood Pressure	Resp. Per Min.	Temp.	Pupils	Reflexes	Reason for Taking
W. M.	22	N.S. 1	"Seconal," Nembutal Phenobarbital Codeine	N.S.	16	98	Constricted	Normal	Suicidal
W.M.	51	N.S.	Barbital	110/64	20	98	Normal	Normal	Suicidal
W.M.	53	N.S.	N. S.	112/90	20	98.6	Normal	Normal	Accidental
W.F.	62	12	Phenobarbital	165/65	22	99	N.S.	Hyperactive	Accidental
W.F.	83	N.S.	Phenobarbital	140/60	20	99	Normal	Normal	Accidental
W.M.	23	N.S.	N.S.	130/90	20	99	Constricted	Absent	Suicidal
W.F.	65	N.S.	N.S.	N.S.	N.S.	N.S.	Normal	Normal	Accidental
C.M.	5 Wks.	N.S.	N.S.	N.S.	N.S.	98	N.S.	N.S.	Accidental
W.F.	32	N.S.	N.S.	100/72	14	N.S.	N.S.	Normal	Drug Addict
C.M.	14	54	Nembutal	115/80	20	98.6	Normal	Normal	Accidental

*W.F., white female
W.M., white male
C.F., colored female
C.M., colored male
*N.S., not stated

Table 1

venous drip of normal saline) at the rate of 1 c. c. or 3 mg. per minute until the effects of this stimulus begin to show in the form of tremors of the extremities, twitchings of the lips and eyelids and movement of the eyes.[4] As soon as this stage has been reached, the dose is decreased in frequency so that the patient is kept at the level of minimal motor activity, for at this level the respiratory and cardiac centers are receiving the maximum stimulating effect of the drug. Usually it is necessary to give about 1 c. c. every five minutes to keep a patient at this level. As the effects of the barbiturate wear off, the frequency of administration of picrotoxin is slowly diminished to once every ten minutes and then every fifteen minutes, and is discontinued entirely when the patient is sufficiently restless to move about in bed and responds to minimal external stimuli.

(3) Circulatory collapse should be anticipated for the first 24-48 hours and shock treatment carried out.

(4a) Patent airway should be assured by the frequent suction of mucus. Dentures should be removed and the tongue must be kept forward.

(b) The foot of the patient's bed should be elevated to prevent aspiration pneumonia.

(c) The patient should be kept warm. Do not use too much heat as it may accentuate shock.

SUMMARY

(1) From 1938 to 1943 inclusive there were 49 admissions for acute barbiturate poisoning to Charity Hospital, New Orleans. Five or 9.8 per cent of these cases proved fatal.

(2) Eighteen took the drug with suicidal intent and thirteen accidentally.

(3) Diagnosis is difficult when the history of ingestion cannot be ascertained and when gastric lavage fails to reveal telltale undigested colored capsules.

(4) Treatment should consist of the immediate removal of unabsorbed drug from the gastro-intestinal tract, the administration of drugs to counteract the depressant effect on the central nervous system (picrotoxin, caffeine, strychnine, "coramine," and so on), prevention and treatment of circulatory collapse, and measures to prevent secondary infection, particularly bronchopneumonia.

BIBLIOGRAPHY

1. McDaniel, F. L.; and Bell, R. A.: Barbiturate Poisoning: A Review with Report of Two Cases. U. S. Naval Med. Bull., **36**:32, 1938.

2. Goodman, L.; and Gilman, A.: The Pharmacological Basis of Therapeutics. New York: The Macmillan Co., 1941.
3. Fantus, B. (in collaboration with Richards, R. K.): Therapy of Cook County Hospital: The Therapy of Barbiturate Poisoning. J.A.M.A., 115:527, 1940.
4. Bleckwenn, W. J.: and Masten, M. B.: The Antidotal Treatment of Barbiturate Intoxication. Report of Treatment with Picrotoxin in Six Cases. J.A.M.A., 111:504, 1938.

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NUTRITIONAL DEFICIENCY AS AN ETIOLOGICAL FACTOR IN ICTERUS ACCOMPANYING PNEUMONIA IN THE NEGRO*

II. VALUE OF BREWER'S YEAST IN PREVENTING ICTERUS IN PNEUMONIA

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During the period 1936-38 Turner et alii[1] observed an incidence of 67.7 per cent icterus accompanying lobar pneumonia in a group of seventy-four cases of Negro adults in George W. Hubbard Hospital. Numerous authors (Christian,[2] Elton,[3] Bianchi,[4] and Maugeri[5]) have reported a higher incidence of icterus accompanying pneumonia in Negroes as compared to whites. The authors undertook a series of studies on normal Negroes to determine whether there was a detectable physiological basis for this difference. Erythrocyte and leukocyte counts, hemoglobin determinations, bleeding time, coagulation time, and corpuscular fragility tests were made and all findings in the group reported to be within accepted physiologic values.[6]

Subsequent observations indicated that the patients in whom this high incidence of icterus had been noted were observed during depression years when the incidence of unemployment was high and evidence of considerable malnutrition was encountered in the group. It was established that many of the individuals in this series of patients had been living upon diets limited to fat "side meat," corn meal, overcooked turnip greens, and sorghum. Such a diet is excessively rich in fat, relatively low in protein and deficient in the vitamin B complex.

Rich and Hamilton,[7] Gyorgy and Goldblatt[8] and others have demonstrated that deficient diets can produce definite pathological changes in the liver. These observers noted that the liver changes could be prevented by the use of vitamin B complex. Patek and Post[9] have shown that adequate diets high in protein, carbohydrate and vitamin plus large doses of brewers' yeast tend to improve patients with hepatic cirrhosis. Snell[10] has also shown improvement of cirrhosis with high carbohydrate diets accompanied by high vitamin intake.

Following the line of investigation suggested by these studies the authors[11] placed a series of dogs on diets similar to those utilized by the patients and subsequently induced pneumonia in these animals. Eight control animals were fed on adequate diets while fourteen animals were restricted to diets of fat "side meat" (pork), corn meal, overcooked turnip greens, and sorghum. All animals were carefully checked for van den Bergh reactions before and during the experimental production of pneumonia. At intervals of 21 to 55 days from the time the animals were placed on the control and restricted diets pneumonia was artificially induced. The lungs were insufflated with a mixture of 6.0 c.c. of equal parts of 8 per cent mucin and 24-hour blood broth cultures of pneumococci (Type I Robertson strain) suspended in 15 c.c. of autogenous blood. Van den Bergh tests were made twice daily on all animals in the two groups following insufflation of the lungs. All animals were subsequently sacrificed and autopsied. In the period between insufflation and death, none of the eight control animals developed positive van den Bergh reactions while nine of the fourteen animals on restricted diets developed positive van den Bergh reactions. This investigation indicated that experimental pneumonia in the dog produces an increase in the serum van den Bergh when it is superimposed upon a nutritional deficiency. The experimental dietary conditions parallel those established to exist by careful clinical investigation in the group

*Received for publication August 3, 1945.
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of Negro patients with both pneumonia and jaundice referred to above.[1] It was therefore concluded that there is a definite relationship between dietary deficiencies and jaundice in the patient with pneumonia. It seemed probable that this relationship was responsible for the high incidence of jaundice observed in Negro patients with pneumonia at Hubbard Hospital rather than any racial predisposition.

In view of the reports of Gyorgy and Goldblatt[8] and Patek and Post[9] the authors felt that the study would be most satisfactorily continued if a series of dogs could be placed on the same deficient diets and then given adequate supplementary amounts of vitamin B complex prior to, and following, the artificial induction of pneumonia. The present paper is a report of the results of this study.

Twenty young dogs not more than one year old were selected from the college dog pool. Nine dogs (*Table 1*) were placed on the restricted diet only. The remaining eleven (*Table 2*) were on the same diet to which was added brewer's yeast. All food consumption was measured accurately, records being kept of all food intake and any food rejection. The brewer's yeast was mixed with the fat "side meat," boiled turnip greens, corn meal, and sorghum. After they had been on this regime for from 21 to 49 days pneumonia was induced by insufflating the lungs with 5.0 c.c. of equal parts of 8 per cent mucin and 24-hour blood broth culture of pneumococci (Type I Robertson strain) in 15 c.c. of autogenous blood. The mucin was used as an aid in the experimental production of pneumonia as suggested by Nungester and Jordenais.[12] Van den Bergh tests were made at daily intervals before insufflating the lungs and twice daily following insufflation. The animals were subsequently killed and autopsied at intervals of from one to four days following insufflation.

Table 2 summarizes the procedures and observations made in this group of eleven dogs receiving brewer's yeast in addition to the restricted diet. It will be noted that none of the animals on the restricted diet plus brewer's yeast developed a positive van den Bergh reaction while all nine of the control animals on the restricted diet without brewer's yeast (*Table 1*) developed positive van den Bergh reactions. Another observation of some interest is that all of

DIETS RESTRICTED TO FAT MEAT, TURNIP GREENS (BOILED), CORN MEAL AND SORGHUM (CONTROL GROUP)

Dog Number	Weight at Beginning of Experiment	Weight at End of Experiment	Number of Days on Diet Before Inducing Pneumonia	van den Bergh		Observation on Autopsy	
				Before Pneumonia	After Inducing Pneumonia	Lungs	Liver
22	7.30 K	6.10 K	21	Negative	Positive	Diffuse pneumonia	Generalized fatty degeneration
24	5.34 K	4.54 K	47	Negative	Positive	Massive pneumonia	Marked bile stasis and fatty degeneration
29	6.82 K	6.10 K	28	Negative	Positive	Pneumonia, right lung	Extensive fatty degeneration
30	6.36 K	4.55 K	49	Negative	Strongly positive	Advanced pneumonia	Diffuse fatty changes. Fatty necrosis of liver
31	5.00 K	3.30 K	35	Negative	Positive	Marked congestion	Marked fatty degeneration and necrosis
33	5.70 K	5.00 K	42	Negative	Strongly positive	Massive lobar pneumonia	Diffuse fatty degeneration of liver cells
40	4.02 K	3.75 K	34	Negative	Strongly positive	Lobar pneumonia	Marked fatty degeneration and necrosis
41	3.52 K	3.30 K	34	Negative	Strongly positive	Lobar pneumonia	Extreme fatty necrosis of the liver
42	2.84 K	2.30 K	28	Negative	Positive	Lobar pneumonia	Diffuse generalized fatty necrosis

Table 1

the animals on the restricted diet alone lost weight during the experimental period while seven of the eleven animals on the restricted diet plus brewer's yeast did not lose weight and five of them actually gained. The control group lost a total of 7.86 kilos or an average of 0.87 kilo per dog during the period while those fed on restricted diets plus brewer's yeast as a group gained 0.5 kilo. Throughout the feeding period the animals in the latter group rejected very little of their food and after the first day or two seemed to eat with relish while the dogs not receiving brewer's yeast rejected more and more of their food as time went on and seemed to have little appetite for it.

On pathological examination all but one of the control animals had developed a clear cut pneumonia and all nine controls showed extensive fatty changes in the liver. While the eleven animals fed on the restricted diet plus brewer's yeast developed pneumonia, the reactions were less severe and there was no evidence of pathological changes in the liver of animals 48, 59, 61, 63, and 65. Only one animal, number 57, showed marked degenerative changes in the liver comparable to those observed in the control group.

SUMMARY

(1) Nine dogs fed on diets restricted to fat meat (pork), overcooked turnip greens, corn meal, and sorghum all developed positive van den Bergh reactions after the artificial induction of pneumonia. These animals all had marked fatty degenerative changes in the liver on pathological examination.

(2) Eleven dogs fed on similar diets plus brewer's yeast failed to develop positive van den Bergh reactions after artificial induction of pneumonia. The lung changes in this group were

DIETS RESTRICTED TO FAT MEAT, TURNIP GREENS (BOILED), CORN MEAL, SORGHUM PLUS BREWER'S YEAST

Dog Number	Weight at Beginning of Experiment	Weight at End of Experiment	Days on Diet Before Inducing Pneumonia	Days of Pneumonia	van den Bergh		Observation on Autopsy	
					Before Pneumonia	After Inducing Pneumonia	Lungs	Liver
47	7.5 K	7.3 K	40	1	Negative	Negative	Early pneumonia	Foci of recent hemorrhage and moderate hyperemia
48	6.5 K	6.8 K	40	4	Negative	Negative	No pneumonia; only slight hemosiderin deposit	No necrosis
53	4.4 K	5.5 K	36	3	Negative	Negative	Bronchopneumonia	Hyperemia and slight necrosis
54	5.5 K	6.4 K	39	2	Negative	Negative	Bronchopneumonia	Very slight fatty metamorphosis and considerable glycolysis
57	6.4 K	6.2 K	40	2	Negative	Negative	Massive pneumonia	Marked fatty metamorphosis and necrosis of marginal portion of lobules
59	9.2 K	7.7 K	36	2	Negative	Negative	Bronchopneumonia	Slight central hyperemia; no degenerative changes
61	9.6 K	10.0 K	40	2	Negative	Negative	Massive recent hemorrhage	No degenerative changes
62	4.3 K	4.3 K	34	3	Negative	Negative	Acute pneumonia massive exudate in alveoli and bronchioles	Slight necrosis and fatty metamorphosis of cells in portal area
63	9.1 K	10.0 K	35	3	Negative	Negative	No pneumonia	Normal
65	7.3 K	7.3 K	35	3	Negative	Negative	Acute broncho-pneumonia	No fatty metamorphosis
66	4.8 K	3.6 K	34	3	Negative	Negative	Bronchopneumonia	Moderate fatty metamorphosis and necrosis of cells in portal area

Table 2

far less severe than in the control group and only one animal in this series exhibited marked fatty degenerative changes in the liver on pathological examination.

(3) The authors have previously noted an unexplained high incidence of jaundice in Negro patients with pneumonia whose diets were known to be similar to the restricted diets used in this study.

CONCLUSION

(1) It seems, therefore, that inadequate diets, particularly lacking in vitamin B complex, render the liver of the dog more vulnerable to the effects of pneumococci when pneumonia is artificially induced.

(2) Adequate quantities of brewer's yeast added to the inadequate diet used in this experiment apparently afford marked protection to the liver in the presence of experimentally induced pneumococcic infection in dogs. The responsible factor may be the vitamin B complex which is abundant in brewer's yeast.

(3) Experimental results parallel the clinical observations upon a group of Negro patients and support the conclusion reached by the authors in an earlier paper that the icterus observed in the group of Negro pneumonia patients who had been on restricted diets was the result of nutritional deficiency.

REFERENCES

1. Turner, E. L.; Bent, M. J.; Holloway, G. D.; and Cuff, J. R.: Icterus Complicating Lobar Pneumonia in the Negro Patient. J.N.M.A., **34**:47-52, 1942.
2. Christian, H. A.: Osler's Principles and Practice of Medicine, 13th Edition, p. 20. New York: D. Appleton-Century Co., 1935.
3. Elton, N. W.: Physiology, Correlations and Technic of van den Bergh Reactions, Icterus Index and Quantitative Serum Bilirubin. Jour. Lab. and Clin. Med., **17**:1-13, 1931.
4. Bianchi, G. S.: Sulla potogenesi dell ittero'nellaopolmonite. Riv. ops., **24**:447-451, 1934.
5. Maugeri, S.: Die pulmonogene Entstehung des Ikterus. Beitrag zur Kenntnis der extrahepatischen Bilirubinbildung. Beitr. Z. path. Anat. u.z. Path., **86**:375-386, 1931.
6. Turner, E. L.; Bent, M. J.; Grant, W. H., and Holloway, G. D.: Icterus Complicating Pneumonia: Corpuscular Fragility in the Normal Negro. Proc. Soc. Exp. Biol. and Med., **37**:481-483, 1937.
7. Rich, A. R.; and Hamilton, J. D.: The Experimental Production of Cirrhosis of Liver by Means of a Deficient Diet. Bull. Johns Hop. Hosp., **56**:185, 1940.
8. Gyorgy, P.; and Goldblatt, H.: Hepatic Injury on a Nutritional Basis in Rats. Jour. Exper. Med., **70**:185, 1939.
9. Patek, A. J.; and Post, J.: Treatment of Cirrhosis of the Liver by Nutrition Supplements Rich in Vitamin B. Complex. Jour. Clin. Invest., **20**:481-505, 1941.
10. Snell, A. M.: Recent Advances in Treatment of Hepatic Disease. Minnesota Med., **23**:551-556, 1940.
11. Turner, E. L.; Bent, M. J.; Holloway, G. D.; Cuff, J. R.; and Quinland, W. S.: Nutritional Deficiency as an Etiologic Factor in Icterus Accompanying Pneumonia in the Negro. Sou. Med. Jour., **36**:603-608 (September) 1943.
12. Nungester, W. J.; and Jourdonais, L. F.: Mucin as an Aid in Experimental Production of Lobar Pneumonia. Jour. Inf. Dis., **59**:258-265, 1936.

SOME NEWER ASPECTS OF ERYTHROCYTE FORMATION AND ITS CLINICAL SIGNIFICANCE*

PRELIMINARY NOTE

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Since the first description of the red blood cell, the mechanism of its formation has been obscured in a haze of theories. Even today the assumption of the development of the mature red cell from a normoblast, through the stage of reticulocytosis is a theory only. The writer attempts here to prove that the mature red blood cell does not stem from a normoblast and reticulocyte. Thus by negation, some light may be thrown upon the subject. The author, also wishes to point out that when the mechanism of red cell formation is clarified, it will enormously aid our management of the various anemias.

There are many theories of the origin of the red blood cell. Downey's "Handbook of Hematology"[1] summarizes a few of these:

(1) Weber believed the fat globules of the liver became transformed into red cells.

(2) Jones and Drummond asserted that the nuclei of colorless corpuscles through hypertrophy metamorphosed into red corpuscles.

(3) Erb maintained that the nuclei of white cells, broke down into granules and became red blood cells after assuming hemoglobin staining.

(4) Ranvier and Schafer asserted that vasoformative cells, through an endogenous intraprotoplasmic differentiation formed one or more non-nucleated hemoglobin-containing spheres, which were given off in the blood stream as mature red cells.

(5) Heitzmann thought that hematoblasts broke into small pieces, becoming red cells.

These and many other theories are characterized chiefly by the variation and confusion of thought. More modern authors, such as Issacs (1932) noted that red blood cells mature in the adult marrow. Sabin (1928) believed that red blood cells mature in the lumen of the capillaries of the bone marrow. Jorden and Baker (1927) believed that red blood cells are released into the circulation through gaps of the endothelial walls of the capillaries. These authors, as well as most modern writers believe the red blood cell matures from a reticulocyte, which

*Received for publication November 10, 1944.

in turn comes from a normoblast of the bone marrow. But this sequence of development has never been proved.

In order to prove or disprove the development of the red cell, it is first necessary to obtain in the adult, a regeneration of red blood cells. With this in view, the writer presents several cases of pernicious anemia during treatment, in which there was a sustained reticulocytosis at a high level, a level incidentally much higher than can be attained by parenteral liver theory. To achieve this, the hormone addisin was used. Because it is an important factor in this research, let us briefly review the pertinent facts.

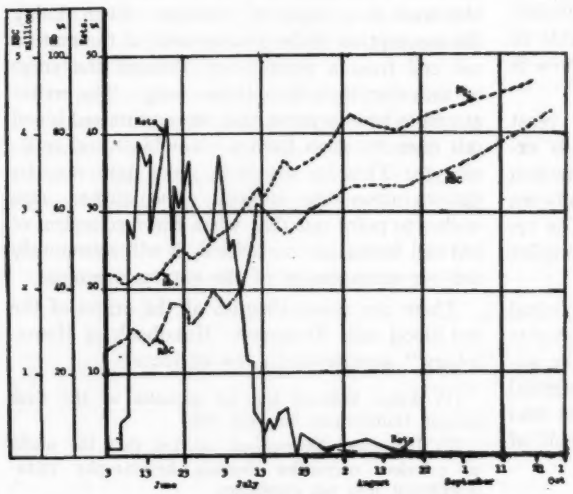

Fig. 1, Case 1

A prolonged reticulocytosis is obtained from a single injection of concentrated gastric juice.

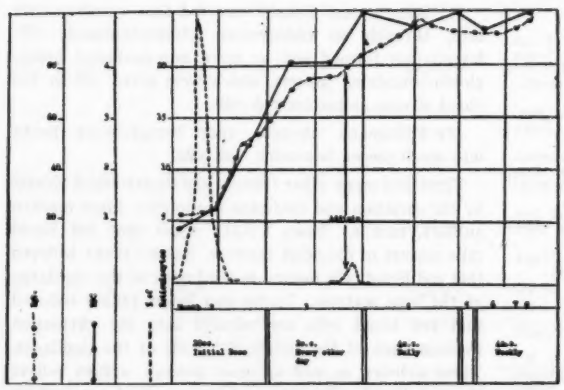

Fig. 2, Case 2

The bone-marrow stimulation by massive doses of parenteral liver[4] produces a high reticulocyte level of short duration.

After Murphy's and Minot's memorable experiments with liver therapy, it occurred to Castle,[2] after incubating beef juice and gastric secretions, that the stomach itself secreted the all important factor. For some reason, after obtaining a mild red cell regeneration in pernicious anemia, by feeding these patients with beef juice and stomach secretion, which had been previously incubated, he went no further in his research.

It occurred to one of us (R.S.M.)[3] that perhaps the factor which Castle designated X, might be a hormone present in the lining of the stomach and in its secretions. We found that the intramuscular injection of concentrated gastric juice produced a sustained reticulocytosis at a high level. It was further discovered, that the hematopoietic substance found in the normal gastric secretion of man, swine, and dogs was thermolabile, dialyzable through collodions and exhaustible. It also withstands chemical treatment known to destroy enzymes. It is therefore a hormone, and we call it addisin, after Thomas Addisin, the first person to describe pernicious anemia.

Fig. 1, Case 1 shows a typical response to the hormone. It should be noted that there was a prolonged reticulocytosis of over thirty days as compared to a reticulocytosis of three to seven days with liver therapy.

Fig. 2, Case 2 reveals the essential difference.[5] It should be noted too, that in both cases the red blood count did not appreciably rise until the disappearance of the reticulocyte.

Fig. 3, Case 1 shows the graphic representation of the marrow activity. Further to note the enormous stimulation of the bone morrow.

Fig. 4, Case 3 discloses a reticulocytosis of sixty days, as compared with a liver response of three to seven days. Even in this case, the total red count during this prolonged bone marrow

stimulation, was only 800,000 R.B.C. per cu. mm.

Fig. 5, Case 3 again discloses the activity of the bone marrow with numerous nuclear particles, nucleated red blood cells and eosinophiles. It is at once evident that these cases would be ideal to study, with the view of attempting to discover the actual formation of the red blood cell.

It is of some importance to discover the order of appearance of the elements of bone marrow activity in the circulation. After the administration of either gastric secretion or liver therapy, the first evidence of marrow stimulation is the appearance of nuclear particles. They may appear as early as thirty-six hours after the administration of the hematopoietic substance. Following these, nucleated red blood cells will appear almost immediately. After an elapse of six to eighteen hours, the reticulocyte appears. It is not until after the disappearance of the reticulocyte that the red blood count begins to rise.

A careful study of these cases reveals some most interesting facts. In all of them, whether liver, or the hormone addisin is used, we note that the total red count does not materially increase until the reticulocyte disappears. Even in *Case 3, Fig. 4,* with a sustained reticulocytosis of over sixty days, the total increase is only 800,000. Subsequently, after the disappearance of nuclear particles, nucleated red cells, and reticulocytes, the red blood count increased to 4,200,000, a total increase of nearly 2,000,000 red cells, or nearly a 100 per cent increase, and in a period of only nine days. If the reticulocyte were, or became red blood cells, the increase should be immediate, from the chart, by the tenth day. For example, in *Fig. 4, Case 3,* the height of the reticulocyte regeneration is 26 per cent. The red cell count, on that day, the sixteenth, after administering the hemotopoietic substance, if the reticulocyte were, or became mature red cells, should be 26 per cent of 2,200,000 or 570,000 red blood cells. The total count should then be 2,800,000 instead of remaining at the 2.2 million level.

The argument may be presented that perhaps Hayem's solution destroys the reticulocyte and therefore in a red blood count by Hayem's

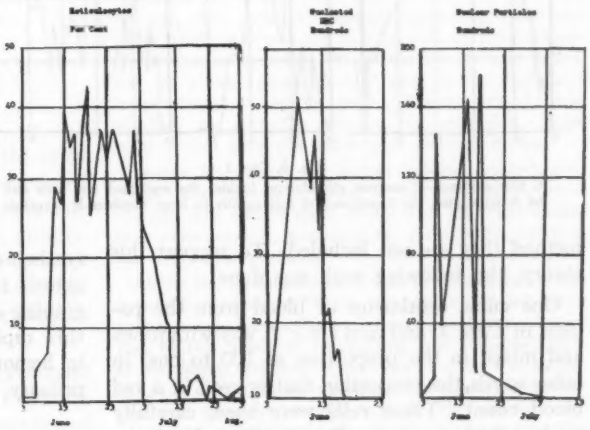

Fig. 3, Case 1

In this graphic evidence of marrow stimulation, it should be noted that nuclear particles and nucleated red blood cells appear in appreciable numbers before the reticulocyte rise.

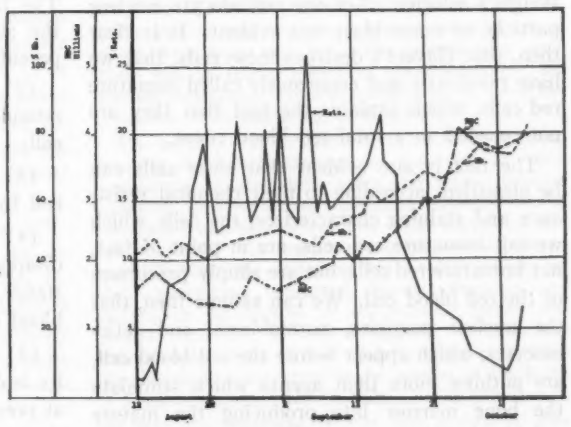

Fig. 4, Case 3

A prolonged reticulocytosis of over 60 days is obtained from a single injection of concentrated gastric juice. It should be noted that the red blood cell count does not show any marked elevation until after the disappearance of the reticulocyte.

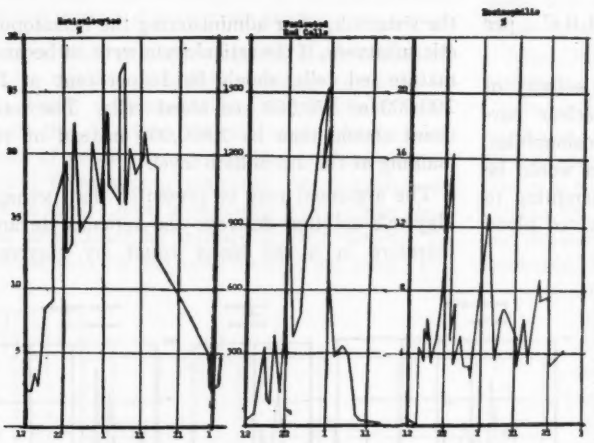

Fig. 5, Case 3

In this evidence of marrow stimulation, besides the nucleated red cells and the reticulocytes, the appearance of eosinophilis in large numbers is revealed.

method they are not included. To support this theory, the following work was done:

One cubic centimeter of blood from the patient of *Case 3,* and also *Case 1,* was withdrawn and mixed in the proportion of 100 to one, in other words the proportion that is used in a red blood count. These cells were then, carefully washed with normal saline, so that all of the Hayem's solution was removed, they were then spread on a slide, stained with a vital stain, brilliant crystal blue, and counter-stained with Wright's solution. Not one reticulocyte, nuclear particle, or normoblast was evident. It is clear then, that Hayem's destroys these cells, that we have previously and erroneously called immature red cells, which explains the fact that they are not counted in a total red blood count.

The fact is also evident that since cells can be classified, according to their chemical resistance and staining characterizes, the cells which we call immature red cells, are in point of fact, not immature red cells, but are simply precursors of the red blood cell. We can assume then, that the nuclear particles, normoblasts, and reticulocytes, which appear before the red blood cell, are nothing more than agents which stimulate the bone marrow into producing the mature red blood cell.

From a practical view point, what then is the significance of these facts? It is at once evident that the normoblast, the nuclear particles, and the reticulocytes contain in themselves, some agent different from the hormone in the gastric juice which Castle called factor X, which stimulates their appearance in the blood stream. This agent is at present unknown, but it is probably a hormone. When this factor is isolated from the reticulocyates, nuclear particles, and normoblasts, it will be capable of causing an immediate regeneration of red blood cells. From a practical viewpoint, we can see how important this will be in its clinical application. It will mean that the administration of liver, gastric secretions, or any hematopoietic substance will be unnecessary and that it will not be necessary to wait for the stage of reticulocytosis to appear and disappear before the beginning of a red cell rise. A red cell increase of this rapidity will be of enormous importance in hemorrhage of any type, as well as in any primary, macrocytic anemia.

CONCLUSIONS

(1) The unknown substance which Castle termed X, is the hormone addisin, and is present in the gastric secretion of swine, dogs and man. The fact that it is stored in the liver, assures the success of liver therapy, both orally and parenterally.

(2) The nuclear particles, normoblasts and reticulocytes are precursors of the mature red cell.

(3) But they are unrelated to the red blood cell by chemical and staining identification.

(4) In themselves, by this appearance and disappearance they probably liberate some substance, which stimulates the formation of the red blood cell.

(5) This substance is at present unknown, but its isolation will enormously shorten the time at present required for red blood cell regeneration.

BIBLIOGRAPHY

1. Downey, Handbook of Hematology. New York: Paul B. Hoeber, Inc., 1938.

2. Castle, W. B.; Heath, C. W.; and Strauss, M. B.: Amer. J. Med. Sci., **182**:741-746 (Dec.) 1931.
3. Morris, R. S.; Schiff, L.; Foulger, J. H.; Rich, M.; and Sherman, J. E.: J.A.M.A., **100**:171 (Jan.) 1933.
4. Riddle, M. C.; and Sturgis, C. C.: Amer. J. Med. Sci., **180**:—, (July 1) 1930.
5. Sherman, J. E.: Sou. Med. Jour., **26**:944-946 (Nov.) 1933, also **28**:1112-1114 (Dec.) 1935.

ACUTE PORPHYRIA*

REPORT OF TWO CASES

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An excessive amount of porphyrin in the urine (porphyrinuria) is found in several unrelated conditions, such as plumbism, sulfonamide poisoning, hemachromatosis, pernicious anemia, chronic alcoholism, and pellagra. The amount of porphyrin found in the urine in these diseases is relatively small and the prophyrinuria is secondary to the primary condition.

In contrast to the secondary porphyrinurias above, porphyria is a primary disturbance of porphyrin metabolism and excessive amounts of porphyrin appear in the urine and elsewhere. Two fairly distinct types of porphyria are recognized. The first is known as congenital porphyria and appears early in life. It is characterized by pinkish discoloration of the teeth, solar dermatitis due to photo-sensitivity, and by large amounts of prophyrin (predominantly uroporphyrin I) in the urine. The second type is known as acute or subacute porphyria and is characterized by severe cramping abdominal pain, symptoms referable to diffuse involvement of the central and peripheral nervous system, and by porphyrinuria, (predominantly uroporphyrin III). In acute porphyria, the porphyrin may not be constantly present in the urine, but it has recently been determined that another substance known as porphobilinogen is more constantly present in the urine of these patients. For a more detailed discussion of porphyria, the reader is referred to the recent review by Nesbitt.[1]

*Received for publication June 23, 1945.

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It has been stated that acute porphyria is a relatively rare condition. The fact that prophyrin is only intermittently present in the urine of patients suffering from acute prophyria sometimes makes the diagnosis difficult, but with the newer evidence that porphobilinogen is more constantly present, diagnosis of this condition may become more frequent. The test for porphobilinogen is simple and is easily performed in the ordinary office laboratory.[2]

Case 1.—A 21-year-old white soldier was well until October, 1943, when he noticed generalized aches and pains which were so mild that he did not report them. On November 2, 1943, he fell on an obstacle course and on arising, complained of pain in the back and lower abdomen. Due to persistent back pain, he was admitted to a station hospital the next day. Some relief of this pain was noted after physical therapy.

During his stay at the station hospital, he began to notice stiffness and progressive weakness of his arms and legs. The records made at this time say: "He became very uncooperative, semi-rational, periodically confused, and a behavior problem."

At the station hospital variations in his condition were noted. It was noted, "When the patient did not know he was being observed he would get up and walk about." Due to this behavior, malingering was suspected early in his illness, and later it was felt that he was suffering from a psychogenic disturbance. Progressive emaciation and muscular atrophy ensued. Hypertension was noted and a roentgenogram of the abdomen revealed a left renal calculus.

In childhood the patient had scarlet fever and diphtheria. There was no history of exposure to any toxic substances or industrial poisons. He had no knowledge of ever having taken sulfonamide compounds.

The patient was the oldest of nine siblings, all of whom were living and well. The parents were well. There was no family history of photo-sensitivity, abdominal complaints, muscular atrophy, or of any other symptoms which might suggest porphyria.

The patient was transferred to O'Reilly General Hospital, Springfield, Missouri, on December 23, 1943, complaining of generalized aches and pains, muscular weakness, and recurrent abdominal cramps. Severe emaciation was present and the facial expression was one of anxiety. The heart was normal. Blood pressure was 156/118. The abdomen was normal except for slight generalized tenderness. Severe weakness and atrophy of the muscles of the shoulder girdles was present bilaterally, as well as general weakness and some atrophy of the muscles of both upper extremities. No abnormality was noted in the muscles of the trunk or lower extremities. No fibrillations were present and the deep and superficial reflexes were normal in spite of the extensive atrophy.

Hematology, sedimentation rate, blood Kahn, and electrocardiogram were normal. Quantitative determina-

tion of blood non-protein nitrogen, urea, creatinine, glucose, albumen and globulin were normal. Routine urinalysis was normal. Shortly after admission, qualitative urinalysis for porphyrins was negative. No examination for porphobilinogen was done at this time. Two cerebrospinal fluid examinations, including Kahn, total protein, glucose, cytology, and gold-sol were entirely normal. No abnormality was noted in the cephalin-cholesterol, van den Bergh or galactose tolerance tests of liver function. An electro-encephalogram suggested generalized cortical damage. Muscle biopsy showed only mild, nonspecific general atrophy.

The muscular atrophy progressed until the upper extremities became flail-like. Cramping abdominal pain was present almost constantly and loops of spastic intestine could be palpated through the abdominal walls. In spite of the general progression of his illness, pronounced variations occurred from time to time so that one day the patient might be bedfast and almost moribund, and the next day be up walking about a little. The tendon reflexes became less active and finally were almost or completely absent in all extremities. On February 8 and 9, 1944, a series of generalized grand mal convulsive seizures occurred. Each seizure lasted three to four minutes and was followed by a period of unconsciousness lasting 10 to 20 minutes.

During an episode of especially severe abdominal cramps, it was noted that the patient's urine was cherry-red in color, and when it was exposed to light it gradually became the color of port wine. These urine specimens were then found to contain uroporphyrin in large amounts and all subsequent urine specimens contained porphobilinogen. Unfortunately, no facilities were available to determine the exact type of uroporphyrin.

Transfer to a Veterans' Facility was effected in March, 1944, and according to reports received the patient died approximately one month later. No information is available concerning necropsy.

Case 2.—A 32-year-old white soldier was in good health until July 15, 1944, when he developed severe dull aching pain across the upper abdomen. At times the pain was cramping in nature and would seem to migrate from the right lower quadrant to the right upper quadrant and across to the left upper quadrant. Information as to the patient's early course was obtained largely from the transfer records as the patient was irrational during much of that time. In early July, 1944, physical examination was normal except for moderate tenderness of the abdomen, and an erythematous, slightly pruritic, skin lesion on the lower third of the left leg. The severe abdominal pain persisted for ten days during which time routine hematology, urinalysis, and roentgenograms of the gastro-intestinal tract were normal. He was given sulfadiazine for three days and sulfaguanidine for three days without effect. Erythematous skin lesions appeared on the dorsum of both hands and the forehead. These had been excoriated so that massive crusting had ensued. An anxious appearance and a lack of organic signs led to a diagnosis of "simple adult maladjustment" on July 29, 1944. On August 12, 1944, the patient's condition suddenly became much worse and the next day flaccid paralysis of the upper extremities was first noted. Severe anorexia was present. The muscles of the shoulder girdle, the triceps, biceps and wrist extensors were completely paralyzed. There was weakness of the psoas muscles and glutei. No sensory changes were present. On August 16, dysphagia developed. A lumbar puncture on this date was normal except for "heavy increase in globulin," but the gold-sol on this date was normal. He was evacuated to another hospital due to imminent respiratory failure.

After evacuation, re-examination on August 17, 1944, disclosed complete paralysis of both upper extremities with the exception of the intrinsic muscles of the hand which showed slight sparing. The biceps and patellar reflexes could not be elicited, but all other tendon reflexes were active. The abdominal and cremasteric reflexes were absent. There were no sensory changes or pathological pyramidal tract signs. A lumbar puncture was performed and showed 48 milligrams per hundred c.c. of total protein and no other abnormality. Twenty minutes after the lumbar puncture voluntary respiration ceased and the patient was placed in a mechanical respirator. Fluoroscopic examination on August 24 showed complete paralysis of both sides of the diaphragm. By August 30 the diaphragm was again moving normally and the patient was removed from the respirator. He had been intermittently incontinent of urine and feces but by September 20 had improved so that there was no longer incontinence of urine and only occasional incontinence of feces. Paralysis of the arms and shoulder girdles and forearms was still present, but the patient could move his wrists and fingers a little more than previously. On September 20 the radial, triceps, biceps, patellar, Achilles, abdominal and cremasteric reflexes were absent, but the patient was able to walk with assistance. He was eventually evacuated to the United States and on January 4, 1945, to O'Reilly General Hospital, Springfield, Missouri.

The past history was non-contributory. The mother had died of "locked bowels" but there was no history of her ever passing wine colored urine. A brother had epilepsy and died an accidental death.

On admission the patient was ambulatory but both upper extremities were flail-like. The skin was clear but there were atrophic scars on the forehead, the dorsa of the hands, and the anterior surface of the right leg. He was able to abduct weakly, flex and extend the shoulders to about three-fourths of the normal range. The triceps and biceps muscles, finger and wrist flexors, were moderately weak, and there was complete wrist drop and paralysis of the extensors of the fingers. Mild paresis of the flexors and extensors of the ankles was present. The gait was a waddling "dystrophic" type. Triceps, biceps, radial, ulnar, patellar, and hamstring reflexes were hypoactive, the other tendon reflexes being normal. Abdominal reflexes were present and the cremasterics absent. There were no pathological reflexes and no sensory changes.

Muscle biopsy from an atrophic area was normal. Lumbar puncture showed a fluid entirely normal except for a total protein of 40 milligrams per cent. Electro-

encephalogram, blood Kahn and hematology were normal. Urinalysis was normal except for the constant presence of porphobilinogen. No porphyrin was found at any time.

The patient showed slight improvement in the strength in the upper extremities and the gait became more normal.

COMMENT

It should be noted that in both of the above cases psychogenic disturbances and even malingering were suspected, until muscular atrophy and paralysis appeared. The tendency to misdiagnose these cases as psychoneuroses is easy to understand. The abdominal complaints are entirely out of proportion to the physical findings. In fact, the physical and laboratory findings are usually nihil as far as explaining the abdominal complaints. Exploratory laparotomies have sometimes been done upon patients with acute porphyria and if nothing is found, psychoneurosis is then more strongly suspected. In addition, mental symptoms suggestive of a psychoneurosis may develop as a result of the same cerebral irritation which may later produce delirium and convulsions. The pronounced day-to-day variation in the patient's condition; his anxious appearance and the fact that he may become a "behavior problem" because he obtains no relief from his symptoms, may frequently lead unwary examiners to suspect malingering or psychoneurosis. Remissions are not infrequent in acute porphyria, and it is possible that some patients who never developed obvious demonstrable abnormality in neuromuscular function are still masquerading as psychogenic disturbances.

The diagnosis of infectious neuronitis (Guillaine-Barré) syndrome was suspected in the second case, but aside from the subjective and rather unreliable report of "heavy increase in globulin," no significant elevation of total protein of the spinal fluid was ever demonstrated.

It is noteworthy that porphyrinuria apparently never occurred in *Case 2*, or occurred so transiently that it was not observed. This suggests the distinct possibility that some of the undiagnosed muscular atrophies seen in the past may have been cases of acute porphyria with porphyrinuria present only intermittently. In the future, examinations of obscure muscular disorders should include urine examination for porphyrin and porphobilinogen.

SUMMARY

Two cases of acute porphyria are presented. These were characterized by rather sudden onset of acute abdominal pain followed after an interval by muscular paralysis and wasting which showed some predilection for the upper extremities and particularly the shoulder girdles. The deep reflexes were not so depressed as would be expected from the degree of atrophy. One patient developed hypertension and convulsions. The disease may easily be mistaken for a psychogenic disturbance by an unwary examiner. Examination of the urine for porphobilinogen is recommended in obscure muscular atrophies.

REFERENCES

1. Nesbitt, Samuel: Acute Porphyria. J.A.M.A., **124**:286-294 (Jan. 29) 1944.
2. Todd, J. C.; and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods. 10th Edition, p. 117. Philadelphia: W. B. Saunders Co.

MARCH HEMOGLOBINURIA*

WITH TWO CASE REPORTS

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March hemoglobinuria is a rare condition characterized by the passage of red urine containing hemoglobin in solution after physical exertion. In 1941, Gilligan and Blumgart[1] reviewed the literature, discussed the clinical characteristics, blood metabolism and mechanism of march hemoglobinuria and reported three new cases. Forty other case reports were then available, mainly in the German literature. These authors expressed the opinion that march hemoglobinuria occurs more commonly than is generally realized. They suggested that the participation of such a large number of young men in the strenuous exertion of military training, under close medical supervision, would probably result in the discovery of more cases in the future.

*Received for publication June 10, 1945.

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Since their article was published three cases have been reported,[2 3] one soldier in the Australian and two soldiers in the Canadian army. We have encountered two soldiers with march hemoglobinuria at the Regional Hospital, Fort Bragg, North Carolina, and as best we can determine these are the forty-seventh and forty-eighth cases to be reported. Because of the rarity of reported cases and the fact that march hemoglobinuria is rarely thought of when a patient presents himself with the complaint of passing red urine, we feel that the addition of two cases to the literature is desirable, to have them on record, and to re-emphasize the fact that this disorder does occur.

CASE REPORTS

Case 1.—A twenty-year-old white soldier was admitted to the hospital August 23, 1943, with the complaint of passing dark urine after exercise. He was a native of South Carolina and had lived there until he enlisted in the army on January 27, 1941. After he finished high school he worked as a carpenter, as a grocery clerk, and for four years before entering military service, as the driver of a delivery truck for a dry cleaning establishment, but he denied contact with chemicals ordinarily used in the latter business. There was no history of syphilis in the patient or his family. He was married in January, 1942, and his wife had a miscarriage in the fourth month of pregnancy. Personal and family history was otherwise irrelevant. The soldier had his army training, including full basic, in southern states and enjoyed excellent health. He arrived in England August 24, 1942. About three weeks after disembarking he began marching and drilling seven or eight hours a day. On September 28, 1942, after a march of several hours, he noticed that his urine was dark red, and the urine passed for the next eight hours remained darkly colored but returned to normal color in about twelve hours. There were no associated symptoms. After this attack, each time he performed moderate physical activity for one to two hours this sign would recur. He was admitted to an overseas hospital on January 18, 1943, and returned to the United States as a patient in April, 1943. He was returned to duty on July 6, 1943, but did no strenuous duty until August 23, 1943. On this date he moved several beds up flights of stairs and within two hours after beginning this work his urine was dark red. The patient had no other complaints and considered himself in excellent health.

Physical examination was entirely negative. The orthopedic consultant reported a normal posture and skeletal system. A urinalysis the day after admission to the hospital showed three plus albumin, a positive benzidine test, and 2-3 granular casts and 8-10 white blood cells per high power field. Subsequent urinalyses obtained when the patient was at rest were normal. Several blood counts were normal. Roentgenograms of the chest, skull, dorsal and lumbosacral spine were negative; there was no evidence of lordosis or kyphosis. An intravenous urogram showed prompt excretion bilaterally and normal kidney pelves and calyces. An upright film showed the right kidney to move downward the width of two vertebrae but transportation of the dye to the bladder was normal and there was no kinking or obstruction of the ureter. A cystoscopic examination and retrograde pyelogram performed after moderate exercise showed nothing abnormal except dark red urine which had "the appearance of hemoglobinuria rather

LABORATORY FINDINGS IN THE TWO CASES REPORTED

		Case 1	*Case 2*
Blood—Erythrocytes		4,410,000	5,030,000
Hemoglobin (photoelectric)	per cent	98	85
Leukocytes		8,400	6,900
Polymorphs	per cent	72	68
Lymphocytes	per cent	27	27
Monocytes	per cent	1	0
Eosinophils	per cent	0	5
Reticulocytes	per cent	1.6	1.0
Platelets		259,000	258,000
Blood smears		normal	normal
Clotting time (venous)	min.	4-9	3½
Bleeding time	min.	2½-7½	2
Clot retraction		normal	——
Fragility test		normal	normal
Icterus index (basal)		9-11	8
N.P.N.	mgms. per cent	36	42
Creatinine	mgms. per cent	——	1.8
Calcium	mgms. per cent	10.8	11
Phosphorus	mgms. per cent	3.7	4
Cholesterol	mgms. per cent	227	216
Wassermann		1 negative	——
Kahn		2 negative	2 negative
Donath-Landsteiner test		negative	negative
Acid hemolysin test (Ham)[4]		negative	negative
Serum proteins	per cent	7.4	8.2
Albumin	per cent	5.2	——
Globulin	per cent	2.2	——
A/G ratio		2.3	——
Kidney function—PSP—30 min.	per cent	70	30
2 hours	per cent	95	78
Urea clearance (per cent of average normal)		98	70
Liver function, cephalin flocculation		negative	negative
Basal metabolic rate	per cent	—12	—16
Gastric analysis		normal	normal

Table 1

than hematuria" escaping from each ureteral orifice. Other laboratory data are summarized in *Table 1.*

The patient was asked to walk at a normal pace in the hospital corridors for 1 to 2 hours on several occasions and each time an attack of hemoglobinuria was produced. In two typical experiments the urinalyses before and after exercise are recorded in *Table 2.* Exercising the patient for two hours on his back failed to produce any abnormal physical and chemical urinary changes and exposure of the patient's feet and hands to ice water for 30 minutes did not produce a paroxysm of hemoglobinuria. When contact was lost with this soldier this condition had existed for over a year but there was no evidence that he could tolerate more exercise without hemoglobinuria resulting.

Case II.—A twenty-three-year-old male, native of Pennsylvania, was admitted to the hospital March 8, 1944, with the complaint of passing dark red urine after several hours of strenuous exercise. This soldier enjoyed excellent health except for measles and mumps in childhood, until the age of 16, when in May, 1937, he began working as a messenger boy for a telegraph company. Three days after beginning to walk long distances he experienced severe aching pains in both lower extremities and in about twelve hours his urine was brownish red. All symptoms subsided after two days' rest. Within a period of one month, while doing this type of work, he suffered three similar attacks. In June, 1937, he was admitted to a university hospital*

*Information obtained from this hospital was that this patient was studied as a case of possible paroxysmal hemoglobinuria, and the possibility of syphilis and the effects of exercise were carefully investigated with negative results, and no official diagnosis was made.

URINARY FINDINGS AND ICTERUS INDEX BEFORE AND AFTER EXERCISE (NORMAL WALKING) IN *CASE 1*

	September 17, 1943					Sept. 18	September 30, 1943				Oct. 1, 1943
	Exercise—8:00 to 9:30 A.M.						Exercise—8:00 to 9:00 A.M.				Resting
	Before	After					Before	After			
Time Collected	7:00 A.M.	9:30 A.M.	11:00 A.M.	4:00 P.M.	7:30 P.M.		6:00 A.M.	10:00 A.M.	1:00 P.M.	4:00 P.M.	8:00 A.M.
Color	straw	mahog-any	mahog-any	straw	straw		straw	mahog-any	dark tan	light tan	straw
Reaction	acid	acid	acid	acid	acid		acid	acid	acid	acid	neut.
Sp. Gr.	1.023	1.025	q.n.s.	1.012	1.023		1.020	q.n.s.	1.018	q.n.s.	q.n.s.
Albumin	0	++++	++++	+	trace		trace	++++	++	+	0
Benzidine	0	++++	++++	+	0		0	++++	++++	++++	0
Microscopic	neg.	neg.	neg.	neg.	neg.		neg.	neg.	neg.	neg.	neg.
Icterus Index						15	9	19	22	21	

Table 2

URINARY FINDINGS BEFORE, DURING AND AFTER EXERCISE (NORMAL WALKING) IN *CASE 2*

	April 13, 1944						April 18, 1944				April 19, 1944
	Exercise—8:30 to 11:30 A.M.						Exercise—8:30 to 2:30 P.M.				Resting
	Before	During		After			Before	During	After		
Time Collected	8:30 A.M.	9:30 A.M.	10:30 A.M.	11:30 A.M.	12:30 P.M.	1:30 P.M.	8:30 A.M.	9:45 A.M.	4:45 P.M.	9:00 P.M.	7:00 A.M.
Color	straw	straw	straw	straw	straw	amber	straw	amber	straw	tan	straw
Reaction	acid	acid	alk.	alk.	alk.	alk.	acid	acid	acid	acid	acid
Sp. Gr.	1.016	1.005	1.008	1.014	1.018	1.005	1.021	1.025	1.026	1.028	1.024
Albumin	trace	0	0	0	0	trace	0	+	trace	++	0
Benzidine	0	0	0	+	+	++	0	0	0	++++	0
Microscopic	4-5 WBC h.p.f.	2-3 WBC h.p.f.	3 3 hyal. casts h.p.f.	many amorph. urates	3 hyal. casts h.p.f.	neg.	10-12 WBC h.p.f.	6-8 WBC 1 hyal. cast h.p.f.	loaded with amorph. urates	5 hyal. casts h.p.f.	4-6 WBC h.p.f.

Table 3

where he says that he was told he had hemoglobinuria and that he should avoid strenuous physical activity. For the next five years he experienced no further trouble while he was a student and pressed clothes in a tailoring shop part time. On one occasion during this period he attempted to work as a stock clerk for an electrical company in Philadelphia, which required a considerable amount of walking. A recurrence of the pains and aches in his extremities and dark urine was noted on the first day at this job. In April, 1942, he enlisted in the army and was stationed at a camp in a mid-western state. The first day that he began to exercise to any extent, such as marching or drilling five to six hours, he had a recurrence of the same symptoms. He was hospitalized for investigation and after returning to duty he did no heavy work for three to four weeks. The previously described symptoms immediately returned when he was again subjected to strenuous activity, but from about July, 1942, until January, 1944, he performed jobs compatible with his physical disability and enjoyed good health. In January, 1944, while he was stationed at a camp in California he was required to go through an infiltration course and within a few hours after this exercise his urine was dark brownish red. This soldier arrived at Fort Bragg, North Carolina early in February, 1944. About seven days later he developed symptoms of an upper respiratory infection, without fever or chills. He continued to have a mild non-productive cough until he was admitted to the hospital because of brownish red urine and aching in the extremities that had followed walking many miles the previous day. This patient had never experienced chills, fever, abdominal pain or jaundice with any described attack of his illness. He gave no history of frequency, urgency, nocturia or passage of kidney stones.

Physical examination was entirely negative. A urinalysis done the day after admission was reported as: color, dark brown; reaction, acid; specific gravity, 1.017; albumin, 4 plus; sugar, negative; benzidine test for blood, 4 plus; bile, negative; microscopic, 1-2 coarsely granular casts per h.p.f. A cystoscopic examination and retrograde pyelogram were performed on this same day and were normal except that smoky urine was seen coming from each ureter. On March 13, 1944, the patient developed a cough productive of mucopurulent sputum and had a temperature of 101°. Roentgenogram of the chest revealed a peribronchial (atypical) pneumonia. Following recovery from this conditidon, further investigation of his primary complaint was resumed. Several urine specimens collected while the patient was at rest were essentially normal. Roentgenograms of the skull and dorsolumbar spine revealed no bony changes; there was moderate scoliosis of the dorsolumbar spine. Other laboratory data are summarized in *Table 1*.

The patient's history indicated that it required quite strenuous exercise for a period of several hours to produce an attack of hemoglobinuria. With this in mind we had the patient walk at a normal pace for three hours on one occasion and six hours on another. The urinalyses before, during and after exercises are recorded in *Table 3*. Exposure of the soldier's feet to ice water for 30 minutes failed to produce abnormal urinary findings.

COMMENT

The identification of these two cases of paroxysmal hemoglobinuria as of the "march" variety can scarcely be in doubt. It is regrettable that spectroscopic studies of the serum and urine were not obtainable.

SUMMARY

Two cases of march hemoglobinuria occurring in soldiers are described with detailed clinical and laboratory findings.

REFERENCES

1. Gilligan, D. R.; and Blumgart, H. L.: March Hemoglobinuria; Studies of Clinical Characteristics, Blood Metabolism and Mechanism With Observation on Three New Cases, and Review of Literature. Medicine, **20**:341-395 (Sept.) 1941.
2. Bryce, Lucy M.: March Hemoglobinuria; Description of Features of this Condition and Report of Case. Med. J. Australia, **2**:48-52 (July 15) 1944.
3. Palmer, R. A.; and Mitchell, H. S.: March Hemoglobinuria. Canad. M.A.J., **49**:465-472 (Dec.) 1943.
4. Ham, G. C.; and Horack, H. M.: Chronic Hemolytic Anemia With Paroxysmal Nocturnal Hemoglobinuria (Marchiafava-Micheli Syndrome); Case With Only Occasional Hemoglobinuria and With Complete Autopsy. Arch. Int. Med., **67**: 735-745 (April) 1941.

SURGICAL TREATMENT OF HYPERTHYROIDISM*

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Advances in the knowledge and in the skill of handling patients with thyrotoxicosis have eliminated many of the hazards formerly connected with their surgical treatment. Today, we see little of thyroid crises and other critical states because of better pre- and postoperative management. We have found it unnecessary to do nearly as many stage operations as were done in the past. The discovery of thiouracil has aided further in getting the critical cases of hyperthyroidism into better clinical condition to operate upon safely in one stage with a smoother postoperative course. The introduction of iodine in itself reduced the number of pole ligations and hemi-thyroidectomies greatly. Thiouracil promises more in those with severe thyrotoxicosis.

Hyperthyroidism may be seen in any age

*Received for publication July 27, 1945.

group. Some of the severest cases are found in the young. The most common symptom is the onset of nervousness and irritability, usually associated with increased perspiration and palpitation. They nearly all are much more comfortable in the colder months. Loss of weight is usually found, but is not always present. Those who do not have weight loss usually admit having an increased food intake and energy output. Diarrhea and vomiting may occur with increasing toxicity. The hyperthyroid patient tires easily and muscular weakness may be the presenting symptom. Menstrual changes are noted in a little more than 50 per cent of females, usually causing a more scanty and shorter period.

Examination reveals the typical flushed, moist skin, which may be less in evidence in the elderly. They nearly all show motor restlessness. There is usually a noticeable fullness in the lower neck, which with palpation shows a uniform symmetrical enlargement of the gland. Exophthalmos is seen in 50 per cent of the cases according to Hurxthal[1] and the typical stare and lid lag may or may not be in evidence. The blood pressure is characteristically elevated a little with increase in the pulse pressure. A fine tremor of the hands is noticeable. A true basal metabolic rate will show an elevation which is checked by a blood cholesterol determination. It is unusual to find an appreciably elevated basal metabolic rate without a lower blood cholesterol.

The treatment of hyperthyroidism still remains largely in the realm of surgery, although close cooperation of the internist and surgeon offers the best solution to the problem. Preoperative treatment is of utmost importance. It is the author's opinion that Lugol's solution should be withheld until two or three weeks before operation and thiouracil should be administered in the hospital when possible, because frequent checks on the blood counts and metabolism are advisable.

The preoperative care should include mild sedatives, complete bed rest and hypnotics at bedtime. A high caloric, high vitamin diet should be given. Sweetened fruit juices will be found of aid in getting an adequate amount of carbohydrate in the patient, with consequent fortification of the depleted liver with glycogen. All stimulants are eliminated and visitors restricted. Patients with hyperthyroidism should have a careful evaluation of their cardiovascular system and if there are any signs of decompensation, adequate measures should be instituted by an internist. Finally Lugol's solution (minims ten) is given three times a day until the maximum drop of the basal metabolic rate is received which usually is attained in 10 days to 3 weeks.

Thiouracil represents a great advance in our preoperative preparation of patients with toxic goitres.[2] However, because there are occasional cases that develop toxicity similar to that found in the administration of sulfonomides, it is perhaps best at this time to limit the administration of thiouracil to the most toxic cases. In these, the metabolism can be leveled down to normal or even into myxedematous values.[3] Optimum improvement should be obtained before thyroidectomy. This takes longer when iodine has been given before thiouracil.[4] Whereas, iodine treated patients get an average drop of about 25 points in the metabolic rate, the thiouracil patients get an average of about 50 points, to the region of ± 0. A daily dose of 0.6 gram of thiouracil is given in divided doses of 0.2 gram three times a day. With longer use the metabolism falls lower with this drug, while the maximum drop is received in two to three weeks with iodine and fails to go further down. There seems to be nothing comparable to the iodine escape mechanism in those cases treated with thiouracil. The postoperative course has been smoother with this drug than with iodine.[5] Among the disadvantages of thiouracil are its occasional toxic reactions with leukopenia, increased hyperplasia and increased vascularity of the gland, making the thyroid more difficult to handle at operation. These disadvantages are over-shadowed by its marked effect on the very toxic thyroid patients with high metabolic rates. As with iodine, it is the author's opinion that this drug should be

used at present, only in preparation of patients for surgery.

Choice of anesthesia is of importance. Local infiltration of 1 per cent novocain without epinephrine should be used when there is reduced cardiac reserve or myocardial damage. Gas-oxygen mixtures or even gas-oxygen-ether is satisfactory for the average case. The type of anesthetic should of course depend, somewhat, on the experience of the anesthetist. Cyclopropane may be perfectly safe in some anesthetist's hands, but should not be used by those who are not perfectly familiar with it and use it often. Thyroid patients require a little more in premedication than other cases. However, large doses of morphine are not as a rule employed in preliminary preparation. One and one-half grains of "nembutal" are given at bedtime and may be repeated once if necessary before midnight. Three grains of "nembutal" are given one hour before operation, followed by 1/6 grain of morphine and 1/150 grain atropine one-half hour before surgery. If the patient is to have local anesthesia, scopolamine hydrobromide grains 1/150 is substituted for the atropine. These doses are varied to fit the individual because of differences in toxicity and nervousness, weight, age, and so on.

The head is extended by a sand bag beneath the shoulders. A transverse (Richter) or very slightly curved incision is used. The line of incision is first marked by pressure of a piece of catgut stretched across the neck, midway between the suprasternal notch and the cricoid cartilage. The upper skin flap is dissected up to the level of the cricoid cartilage and the lower flap is carried well down to the suprasternal notch. A vertical incision is made in the mid line through the fascia and preglandular muscles from the cricoid to the suprasternal notch. With this procedure, division of the preglandular muscles is hardly ever indicated and is not done except for removal of very large glands. If the thyroid is very large, we do not hesitate to divide these muscles transversely, at a high level for better exposure.

The capsule is dissected cleanly from the gland and none is removed during the operation. This is of major importance in the prevention of parathyroid tetany. The upper pole is separated carefully with the aid of a gauze pledget attached to a Kelly clamp and a Crile clamp is applied to the superior thyroid vessel from inside out, to avoid injury to the terminal branches of the recurrent laryngeal nerve. The upper pole is always ligated extra capsularly under direct vision. A second hemostat is applied to the lateral vein as advocated by Hertzler[5] and Dinsmore.[6] The third guide hemostat is applied at the inferior pole, leaving some thyroid tissue at this point. The clamp is applied so that it will stand erect in the wound. The poles and lateral thyroid fascia are then divided and an incision is made along the lateral border at the point where the gland is to be divided. Then the gland is turned laterally and the lobe is removed from the tracheal side outward after the manner advocated by Sistrunk.[6] This prevents inserting the hemostat downward toward the tracheo-esophageal groove, again avoiding injury to the recurrent laryngeal nerve. After hemostasis is complete using plain double zero catgut, except for a chromic tie on the superior thyroid vessels, the same procedure is carried out on the opposite side. Mobilization of the second lobe is much easier than the first and it is quickly removed. The sand bag is removed from under the shoulders at this point and the wound is checked for bleeding. Releasing the tension in this way will occasionally show up a bleeder closed off by the pressure of the extended neck. The cervical fascia is closed with a continuous chromic 0 or No. 1 suture, leaving a small rubber tissue drain in the mid line low in the vertical incision. The skin is closed with Michel skin clips.

When the patients have had iodine preoperatively, it has been routine to continue the iodine (minims ten three times a day) for three days postoperatively. When the preparation has been with thiouracil, none has been given postoperatively. The drain is removed in 24 hours, one-half the clips in 48 hours and the remainder of the clips at the end of 72 hours. 2000 to 3000

c. c. of intravenous 10 per cent glucose in normal saline is administered the day of the operation. After that, a satisfactory amount of fluids can be taken by mouth. Fruit juices are given freely for the vitamin C content to insure rapid healing. The head of the bed is raised up in the so-called thyroid position and ice bags are applied to the chest and axillae for 24 hours. Adequate sedation is important and visitors are restricted. A regular high caloric, high vitamin diet is given as soon as tolerated.

Since we are now able to bring about a better preoperative condition of the patients, it is unusual to find oxygen therapy, antipyretics, transfusions and forced feedings necessary. These adjuncts to treatment of the critical cases should of course be kept in mind.

A word may be said here about radiation therapy for treatment of hyperthyroidism. It is our opinion that this should be used only in the very bad risk patients who are thought not to be candidates for surgery because of severe heart disorders or other diseases. The recurrence of symptoms, combined with the occurrence of radiation resistance and resultant difficulty with surgery if it is planned later, outweigh the advantages of this form of treatment. Thiouracil will bring the severe toxic case into such physiological equilibrium that radiation, preoperatively as suggested by Crile,[7] would seem unnecessary.

SUMMARY

(1) Great advances in the preoperative and postoperative management of hyperthyroidism have been made in recent years and have eliminated to a great degree the necessity for stage operations for this condition.

(2) The treatment of hyperthyroidism is still a surgical problem but cooperation with an internist gives the best results, particularly when heart disorders, hepatitis and similar conditions exist.

(3) Thiouracil is proving to be of great help in the preoperative management of hyperthyroidism. Because of its occasional toxic manifestations, its administration should be followed by blood counts frequently. This drug is usually reserved for the severest cases of hyperthyroidism, while Lugol's solution is still used in the preparation of the milder cases of toxic goitre.

(4) Radiation is recommended only for those cases in which operation is deemed inadvisable.

BIBLIOGRAPHY

1. Hurxthal, L. M.: Hyperthyroidism. Surg. Clin. N. Am., **16**:1505-1508 (Dec.) 1936.
2. Astwood, E. B.: The Chemical Nature of Compounds Which Inhibit the Function of the Thyroid Gland. J. Pharmacol. and Exper. Therap., **78**:79-89, 1943.
3. Moore, F. D.; Sweeny, D. N., Jr.; Cope, Oliver; Rawson, R. W.; and Means, J. H.: The Use of Thiouracil in the Preparation of Patients with Hyperthyroidism for Thyroidectomy. Ann. Surg., **120**:152-160, 1944.
4. Bartels, Elmer C.: Thiouracil: Its Use in the Preoperative Preparation of Patients with Severe Hyperthyroidism. Surg. Clin. N. America, 645-650 (June) 1945.
5. Hertzler, A. E.: Technique for Thyroidectomy. Surg. Gynec. and Obstet., **47**:225-234, 1928.
6. Dinsmore, Robert S.: The Technic of Thyroid Surgery. Surg. Clin. N. Am., 1287-1302 (Oct.) 1937.
7. Crile, George, Jr.: Management of the Bad Risk Case. Surg. Clin. N. Am., 1303-1311 (Oct.) 1941.

SPLENIC RUPTURE IN THERAPEUTIC MALARIA*

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Although malarial therapy has been proven to be of great value in the treatment of central nervous system lues, there are certain complications of major importance which occasionally result from its use. Possibly the most spectacular of these, certainly the most serious, is the rare spontaneous rupture of the spleen.

This accident is still rare enough to warrant medical interest when it occurs. Polayes and Lederer[1] reported a total of nine cases of this type, one of which was their own patient. It was their opinion that this complication should be expected more frequently than the general literature at that time implied. All the cases reported by them died as a result of the rupture. Moore[2] in 1943 added to their series two of his own, both of whom expired. He also stated that he knew of no patient who had ever survived the episode. A review of the Anglo-American literature since that time has failed to reveal a recovery from spontaneous splenic rupture due to therapeutic

*Received for publication July 27, 1945.
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malaria, although the literature is dotted with isolated case reports of recovery from the mishap associated with "natural" malaria.

Recently we have had the opportunity to treat a patient in whom this complication had occurred, and who survived splenectomy.

Case Report.—M. F., (*No. C3012*), a white woman, aged 47, was admitted on February 21, 1945, one day after her first chill. A diagnosis of latent central nervous system syphilis having been established, she had received an injection of quartan malarial blood on February 2, 1945. Her general condition was quite satisfactory on admission, her history revealing that she had an attack of malaria as a child while living in the eastern part of Tennessee. There were no detectably enlarged abdominal viscera. A low grade anemia was manifested by a red blood count of 3,200,000 and a hemoglobin (Sahli) of 59 per cent.

During the following twenty-seven days she had chills exactly at three-day intervals during which mouth temperatures of 102-103° F. were recorded. On March 18, she suddenly complained of sharp anterior abdominal pain arising in the left upper quadrant and radiating to the left shoulder. At this time, a friction rub was thought to be heard over the left lower lobe posteriorly. X-ray examination of the chest revealed no abnormalities. In the early morning of March 19, another chill with temperature recording of 104° was noted. Later in the same day, the patient began to vomit all solid foods, the left upper quadrant of the abdomen developing a large tender mass, which was considered to be spleen. The diagnosis entertained at this time was splenic infarct. On March 20, her pain was described as generalized and cramping in nature, and the abdominal tenderness had spread to involve the entire abdomen. She had no chill on this day, but her oral temperature was 101°. On March 21, her generalized cramping pains had become more severe, and the abdominal tenderness was recorded as "exquisite." She was now vomiting all ingested material. Splenic hemorrhage was now proposed as a possibility and a surgical consultation requested.

At the time of the surgical consultation, she was found to be pale, sweating, and thirsty. Her pulse rate was 120 per minute, the blood pressure 120/70, respirations 32 per minute, and rectal temperature 102°. The hemogram revealed a red blood count of 3,140,000, hemoglobin (Sahli) 8 grams, white blood count of 13,480, and a differential of normal distribution. Abdominal examination demonstrated diffuse marked tenderness, most severe over the lower abdomen, no rigidity, active audible peristalsis, and a huge mass in the left upper quadrant, very tender, and conforming in outline and position to the spleen. Rectal examination elicited a boggy tender fulness in the cul-de-sac. Aspiration of the peritoneal cavity established the presence of hemoperitoneum, the aspirate containing 755,000 erythrocytes per cu. mm. A positive diagnosis of ruptured spleen seemed now justifiable.

Following the intravenous administration of 500 c. c. each of blood and plasma, her pulse had receded to 96 per minute, and her skin had become warm and dry. She was now taken to the operating room.

Laparotomy was performed through a left rectus incision under pontocaine spinal anesthesia. Upon opening the peritoneal cavity, approximately 1500 c. c. of blood was discovered. A greatly enlarged spleen (840 grams) presented, with its capsule rolled back, exposing a bare area the size of the opened hand. From this purplish, mushy, and friable surface there were multiple points of sluggish bloody oozing. The ligaments to the organ were divided, and the pedicle divided between clamps and tied with chromic No. 2 catgut. The liver showed no gross abnormalities. Closure of the abdominal wall was effected in layers, with interrupted medium silk sutures throughout. She received 500 c. c. of compatible blood during the procedure, showing no evidence of shock at any time.

Microscopic examination of the specimen showed marked hyperplasia of the pulp, with sinuses packed with cell fragments and pigment.

Her postoperative course was rather uneventful with the exception of a urinary infection which responded promptly. She was ambulatory from the twelfth postoperative day. Termination of her malaria was effected with atabrine and quinine.

The most exhaustive questioning of this patient before and after operation failed to reveal any antecedent traumatism to the chest or abdomen.

COMMENT

Spontaneous rupture of the spleen has been reported occurring with all types of splenomegaly and even in normal spleens, although the malarial spleen is by far the commonest offender. It is probable that this accident, spontaneous and traumatic, will be seen in increasing numbers as a result of the present global conflict. Since the early recognition of the condition provides the only hope of recovery from this usually fatal catastrophe, its possibility should be kept in mind.

BIBLIOGRAPHY

1. Polayes, S. H.; and Lederer, M.: Rupture of the Spleen in Malarial Therapy in Syphilis. J.A.M.A., **96**:1127, 1931.
2. Moore, J. E.: The Modern Treatment of Syphilis. Springfield: Charles C. Thomas, Publisher, 1943.
3. Russ, S. E., and Gaynor, J. S.: Spontaneous Rupture of a Malarial Spleen. J.A.M.A., **127**:758 (March 31) 1945.
4. Wohl, M. L.: Spontaneous Rupture of the Spleen. Ann. Surg., **82**:246, 1925.
5. Aronson, W.; and Fox, R. A.: Spontaneous Rupture of the Pathologic Spleen. Am. J. Clin. Path., **10**:868, 1940.
6. Dudgeon, H. Jr.: Spontaneous Rupture of the Spleen. Sou. Med. Jour., **34**:1247, 1941.
7. Marshall, J. M.: Spontaneous Rupture of the Malarial Spleen. U. S. Nav. Med. Bull., **43**:743 (October) 1944.
8. DeSaram, G. S. W.; and Townsend, R. F.: Spontaneous Rupture of Spleen in Malignant Tertian Malaria. Lancet **1**:584 (May 8) 1943.

ABDOMINAL PREGNANCY*

THREE CASES OF NEAR OR PAST TERM WITH ONE CASE OF EARLY ABDOMINAL PREGNANCY

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Abdominal pregnancy is a rarity in obstetrics. In reviewing the literature I believe this is the largest number of cases, although it is only three, to be presented of advanced abdominal pregnancy in a short period of time on an individual obstetrical service. I wish to emphasize the method of treatment followed and the results obtained.

The first recorded case of extra uterine pregnancy was that of Albucasis, an Arabian physician living in Spain about the middle of the eleventh century. Until 1604, all of the cases on record were those of full term or long retained secondary abdominal pregnancy.

The first operation for extra uterine pregnancy in America was that of Dr. John Bard[1] of New York, who described it in a letter dated December 25, 1759. The second American operation was done by Dr. William Baynham[2] of Virginia in 1791. There were less than ten of these reported in America for almost a hundred years following Dr. Bard's spectacular operation.

Dr. John King[3] of Edistole Island, South Carolina, performed what was termed a "remarkable operation" for abdominal pregnancy in 1816, saving both the mother and child by cutting through the vagina and applying forceps, with abdominal pressure on the fetus from above. This apparently was the first operation for abdominal pregnancy in this country. It was successful, although the method was hazardous.

It was Lawson Tait, in 1883, who thoroughly established the operative treatment of ectopic pregnancy in America. Although confronted by the loss of his first patient he continued to operate and lost only one case out of the next 40. Operative interference was still looked upon with disfavor. The use of galvanic current was advocated by some, even as late as 1890 by Dr. Howard Kelly of Baltimore.

Frequency and Mortality. — According to Schumann, extra uterine pregnancy occurs once in every 300 cases. It is believed that only about 1 per cent of these go to term in the abdomen. Swanson[4] in 1934, reviewing the births in the City of Detroit found there were 10 abdominal pregnancies in 23,248 births or one in about 2,300 births. Of these 10 cases there was a 40 per cent mortality in the mothers and 80 per cent fetal mortality.

Cornell and Lash, in 1933, reported 226 cases of abdominal pregnancy plus ten of their own. They had a mortality of 14.3 per cent but say this could be lowered by not removing the placenta. Beck reports a mortality of 35.8 per cent for operative results in secondary abdominal pregnancy.

Mason[5] reported 66 cases from the English literature plus three of their own with a mortality of 18.8 per cent. They found marsupialization to be the worst method of treatment. Gardner and Middlebrook[6] have added 22 cases recently to the relatively small number thus far recorded in the literature. They found in their review of 258 cases that the incidence is higher above the thirtieth year, but most frequent in the first and second pregnancies.

Primary versus Secondary Abdominal Pregnancy.—Whether there exists such a condition as primary abdominal pregnancy is highly controversial and cannot be definitely settled. The first authentic case was reported in 1896 by Galakin. This case of so-called primary abdominal pregnancy was in the cul de sac. The second case was reported by Witthuser in 1903. This was in the omentum attached to the pelvic organs. The three cases presented might well be called primary, from the placental attach-

*Received for publication July 21, 1945.

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*I wish to acknowledge the valuable assistance and timely suggestions in caring for the patients discussed in this article of Dr. W. T. Pride, Dr. J. R. Reinberger and Dr. Michael Roach, members of the staff of the University of Tennessee School of Medicine and Dr. O. L. Davidson, resident physician at the John Gaston Hospital. Without their help the end results might have been quite different.

*This article was originally to be prepared by the author and Dr. Curtis Ogle, who is now serving with the U. S. Navy in the Pacific area. Due to Dr. Ogle's assignment it became impossible for us to work jointly. I regret that he was unable to contribute, as the contents of this article might have been improved materially with his assistance.

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ments found in each. I am inclined to believe that this term should be dropped. Harrar found only 10 cases in 156,000 pregnancies at the New York Lying-In Hospital of apparent primary abdominal pregnancy and he was of the opinion that these were ruptured secondary pregnancies.

The following criteria satisfy requirements for primary abdominal pregnancy:

(1) Normal looking tubes, ovaries and broad ligaments.

(2) Absence of evidence of penetration between the broad ligaments by the fimbriated extremity of the tubes.

(3) Lack of evidence of escape of the ovum from the uterine cavity.

(4) Absence of interligamentary rupture of the tube.

Who can say that these have all been satisfied at operation which may be many months after a tubal abortion?

Etiology and Race.—Extra-uterine pregnancy has been thought to occur usually due to some malformation or disease of the fallopian tubes. It is well known that there is high instance of pelvic inflammatory disease in the colored race, particularly in the South. And this might be used as explanation for the fact that all of our cases were in the colored race. This is not in accord with the reports of Gardner and Middlebrook who found no racial difference. One of our patients had a large fibroid uterus and it is quite possible that this may have been a contributory factor. It is somewhat difficult to understand how a secondary abdominal pregnancy can follow a primary rupture or abortion from the fallopian tube, implanting itself in a new field where the surroundings are altogether unfavorable. Curtis[7] has explained this on the basis of endometriomatous implants which are present in many pregnant patients. This implant affords a suitbale place for the trophoblast to attach itself and supplies fertile ground for continuing growth of the pregnancy. He and others were able to demonstrate these endometriomatous placques in as many as 20 per cent of autopsies of pregnant women.

Diagnosis.—The inability to diagnose abdominal pregnancy until the fetus has expired contributes largely to the extremely high mortality. Maternal mortality is raised by this, and by improper treatment at the time of operation. The diagnosis can be much easier if the obstetrician will keep in mind the fact that abdominal pregnancy at term can exist. The condition can be detected with surprising accuracy if the obstetrician is suspicious and alert. There are many valuable signs and symptoms:

(1) The general history and laboratory findings consistent with pregnancy.

(2) History in early pregnancy resembling that of tubal rupture, that is, irregular menstrual bleeding, pain, and so on.

(3) The uterus may be felt separate from the abdominal mass, although this is not likely.

(4) Nearness of the fetal parts to the abdominal wall, also the absence of the rounded thick upper pole of the uterus and uterine contractions. The fetal heart tones may be unusually loud. The abdomen at term will probably give the sensation of a generalized fullness, without another well defined body inside the abdomen containing the fetus.

(5) On vaginal examination the cervix will not be much enlarged but will be more firm and in all probability pulled up or pushed further down than normal.

(6) Any fetus lying diagonally or assuming a peculiar habitus should be suspected, especially if diagonally as the enlarged uterus may be enough to push the head or buttocks to one side or the other and allow it to rest in the iliac fossa.

(7) Contrary to the opinion of Mason (1940), I believe x-ray to be of great value, especially in advanced cases of abdominal pregnancy. It is of particular value in determining the abdominal positions as mentioned above and can be useful in hysterography as demonstrated in *Case 2*. The latter however, is not without unattractive features as *Case 2* demonstrates very well a chemical peritonitis encountered following the injection of iodized oil to outline the uterus.

(8) The failure of true labor to ensue after due time and lack of response to medical inductions may be helpful.

TREATMENT

Much progress in the care of extra uterine pregnancy has been made since 1849 when

Meigs[8] wrote in his classical text book on obstetrics,

"For nothing is to be done in these melancholy cases beyond the adoption of mere palliative measures. No man would be mad enough to perform a gastrotomy operation."

The problem of delivering the fetus is usually relatively simple but that of the placenta offers a more difficult decision. There are three methods of approach, namely: (1) marsupialization of the placenta; (2) removal of placenta; (3) or leaving the placenta in place. The first has been discarded by most experienced obstetricians of today because of the greater risk of infection in a wound which may be open for many weeks. To attempt to remove the placenta is placing both the patient and the operator in a dangerous position. On first inspection of the placental attachments, one may feel that the placenta can be removed with ease only to find when it is too late that there was an attachment which was not thought to be present which may involve a vital area. This predicament is not coveted by anyone. Such meddlesome surgery may cost the life of a patient who could have been spared by a more conservative regime.

It is true that the patient may recover more rapidly if the placenta can be removed. The three cases of advanced abdominal pregnancy presented have brought out what seems the more desirable method of caring for the placenta. In these the cord was cut short and tied. As much of the membrane as could be removed was cut away. The placenta was left intact and the abdomen closed tightly without drains. There may arise some complication and it may even be necessary to do a second operation for removal of the placenta as in the case presented by Nicodemus[9] (1940). But this can be done with a greater security later, as the placenta will be in a degenerative stage and possibly detached and lying free in the abdominal cavity. Occasionally suppuration may occur but this can be cared for by simple drainage as was done in *Case 1.*

Since hemorrhage is a primary consideration whatever the approach, the patient should be thoroughly fortified against this prior to operation. Anspach and others have agreed that the optimum time for operation is six to eight weeks after the fetus is known to have expired. This, of course, is desirable if the placenta is to be removed but does not seem necessary in most instances. The placenta will be absorbed by the body if it is given the opportunity and the "hands off" policy is followed.

In reviewing the literature, it was found that on one occasion[10] stilbesterol was used preoperatively and it was thought that this was helpful in bringing about changes in placental blood vessels thereby preventing blood loss. We cannot see the rationale behind this, especially since we do not advocate removal of the placenta. Ware[11] has demonstrated the presence of the gonadotropic hormone in the urine many days after operation if the placenta is left in the abdomen. This has no harmful effects but will prevent lactation as long as the hormone is liberated.

Case 1.—R. S., a colored woman, age 23, gravida 11 para 0, was admitted to the hospital on February 3, 1943. She had not been under the care of a physician during pregnancy. Her estimated date of delivery was February, 1943 (no definite date). She started having pains, assumed to be labor pains, about twenty-four hours prior to admission. First they were approximately 30 minutes apart and they gradually became closer together until they were within one to two minutes of each other. The day before admission she had been seen by a private physician for the first time during her pregnancy.

For the previous ten to fourteen days the patient had a history of many of the classical symptoms of toxemia. Her blood pressure at the out-patient department on the day of admission to the hospital was found to be 170/130. The systolic had dropped slightly by the time she was admitted. She said that the baby had not moved for about 16 hours.

Her history was essentially negative except for a previous pregnancy in 1933 at which time she was delivered of a full term fetus which expired at birth. At this time she had convulsions and said that she was in labor for five days but delivered spontaneously.

Physical examination revealed a blood pressure of 150/130, 99° temperature, 95 pulse rate. There was a tachycardia and accentuation of P 2. The abdomen showed a pregnancy near term. The position was not determined. No fetal heart tones were audible. The impression at this time was: pregnancy, near or at term, pre-eclampsia, non-viable fetus, and questionable labor.

She had a rather marked secondary anemia with a mild leukocytosis. The urine showed three plus albumin, and an occasional fine granular cast. The nonprotein nitrogen was 25 mg. per 100 c.c. of blood. A urine concentration test was run at which time the patient concentrated to only 1.016. A Kahn test was three plus, Frei test negative. During the patient's stay in

the hospital she continued to show a moderately severe secondary anemia. An x-ray of the abdomen was made on February 4, 1943. This showed a single fetus lying transversely with the head on the right.

Abdominal pregnancy was not suspected at first and due to the toxemia which was evident, plus the diagnosis of dead fetus, it was thought advisable to have the patient deliver if possible. First a medical induction was instituted. Since no results were obtained it was decided a bag induction might be done. The patient was prepared for this. On examining the cervix it was found to be enlarged but no fetal parts were felt. However, the os was large enough for the Vorhees bag to be inserted. This was done and distended with sterile saline. After several attempts with no results and inability at all times to feel fetal parts, we became suspicious of the existing condition. It was also noted, with an attempt at bag induction, that a mass would appear just about the symphysis. Later it was obvious that this was the uterus that was being pushed out of the pelvis. A diagnosis of abdominal pregnancy was made. The patient was prepared for a laparotomy and the abdomen opened. A large fetus was removed from the amniotic sac. The fetus was macerated and apparently at term or post mature. The membranes and cord were removed near the placenta, but the placenta was left in place and the abdomen closed.

For many days the patient ran a septic temperature. The incision became infected and drained sero-purulent material. This was thought to be pocketed and a small incision was made over the abscess. The abscess was incised and a large amount of foul smelling pus drained out. A cigarette drain was placed in the incision. A culture was made of this pus which was positive for non-hemolytic streptococci and staphylococci. The patient also developed other complications, namely, ischiorectal abscess which was apparently a flare-up of an old process, and a phlegmasia alba dolens of the left leg. Her course remained septic for many weeks, and she continued to drain a large amount of foul smelling pus from the abdominal incision. She received several transfusions and much supportive treatment. After about two and a half months the temperature subsided and the patient improved very satisfactorily. She was discharged from the hospital in good condition after having spent approximately four months on the ward.

She returned to the Out-Patient Department for the swollen leg mentioned above, but has not been seen since August, 1943.

Case 2.—A. S., a colored woman, age 31, gravida 6 para 5, was admitted to the hospital on September 9, 1943, with the diagnosis of dead fetus. She was admitted from the Out-Patient Department where an x-ray had agreed with the diagnosis. Her last baby was born seventeen months before, and she had not menstruated since that time. She had been under the care of a private physician, and had been told in November, 1942, that she was pregnant. The following March, 1943, she noticed that her abdomen was increasing in size and continued to do so until May, at which time she began to bleed. She continued to bleed until July 17. She was admitted to the hospital in July because of bleeding. She was given a medical induction while in the hospital with no response. She was discharged from the hospital apparently to abort the dead fetus, as she had been diagnosed as a missed abortion. The patient did not return to the Out-Patient Department until September 7, 1943. There had been no fetal movements since May at which time the patient had noticed a cessation of movement and bleeding had begun.

For the previous three weeks she had been having headaches but no other symptoms. She had been admitted to the hospital in September 1942, and discharged with a diagnosis of chronic pelvic inflammatory disease. She had had antiluetic therapy with her first pregnancy.

Her temperature, pulse, respiration and blood pressure were all within normal limits. No significant findings were recorded except for the abdomen where a mass was found to extend to about four fingers above the umbilicus, more to the right side than to the left. This mass was firm and freely movable. There was no tenderness. A vaginal examination the next day revealed a uterus enlarged about the size of an eight weeks prenancy with a mass as described above higher in the abdomen. The impression on admission was mummified fetus and fibroid.

Urine and blood were within normal limits before operation except for mild anemia, and slight albumin in the urine on one occasion.

An abdominal pregnancy was suspected and the uterus was injected with iodized oil a few days after admission. The x-ray findings revealed definite evidence of a dead fetus outside of the uterine cavity and outlined by the iodized oil. The patient developed a peritonitis immediately following the injection apparently due to the chemical which spilled out in the abdominal cavity through the fallopian tube. Operation had to be delayed until this subsided. She was operated upon about one week later.

At operation a macerated fetus, estimated at seven months, was found lying free in the peritoneal cavity surrounded only by the amniotic sac. The uterus was about the size of a six weeks' pregnancy. The placenta was adherent to the sigmoid and several loops of the small intestine. The fetus was removed from the amniotic sac. The membranes and cord were cut close to the placenta and the placenta was left undisturbed. The abdomen was closed and the patient returned to her room in fair condition. Her postoperative course was not remarkable except for temperature elevations at intervals. She was discharged on the thirty-second postoperative day.

She returned to the out-patient department on several occasions. A first visit revealed a mass in the abdomen which was apparently a portion of the unabsorbed placenta. She was not seen again until October 18, 1944. On a check up a cervical smear was positive for gram-negative intracellular diplococci. During this year her menstrual periods have increased in length. Otherwise the patient seems to be progressing satisfactorily.

Case 3.—L. D., a colored woman, age 30, gravida 1 para 0, had been under the care of a private physician who had informed her that she had a transverse position of the fetus and would have to have a cesarean section. She was admitted on February 28, 1944. The expected date of delivery was March 1, 1944. She had had no labor pains but had been having some discomfort. Her past history was non-contributory except for antiluetic treatment for several months during 1944.

Physical examination revealed a normal blood pressure, temperature, pulse, and respiration. The examination was essentially negative throughout except for the abdomen which contained an apparently full term pregnancy. The fetal heart tones were 136 and regular, and the position was thought to be transverse with the head lying in the left lower flank.

The blood and urine examinations were within normal limits. X-ray revealed a single fetus lying diagonally with the head in the left iliac fossa with no evidence of pelvic masses or extra-uterine pregnancy. This was made on February 28, 1944. On further study about one week later, the position of the fetus was essentially the same. However, at this time abdominal pregnancy was suspected and fetal death. The roentgenologist also said that a low abdominal mass could not be excluded.

The patient remained in the hospital for approximately seven days prior to operation. She complained of pains at intervals. On March 7, 1944, a cesarean section was decided upon and done. On opening the abdominal cavity, a full term fetus was found lying free in the abdominal cavity. The cord was cut near the placenta and a living fetus was removed. The placenta was attached to the posterior abdominal wall; about half was between the diaphragm and the symphysis over the inferior vena cava. No part of the placenta was removed. A moderate sized fibroid of the uterus was present. The abdomen was closed and the patient returned to her room.

Her temperature never rose above 101°, returned to normal on the fourth postoperative day, and remained that way until she was discharged on the twenty-seventh day. Unfortunately the fetus lived for only a short period. Thus far we have not been able to observe this patient since her departure from the hospital.

The next case is included for statistical record and because of its unusually rare location. It was not considered in this report as it does not come under the group to which primary consideration was given.

Case 4.—L. B. H., a colored woman, age 23, gravida 3 para 2, was admitted to the obstetrical pavillion, September 1, 1941 at 11:00 p. m. with the complaint of pain in the abdomen and bleeding which had its onset at 2:00 p. m. that day. The pain was of sudden onset in the right lower quadrant which caused the patient to bend forward and confined her to bed. She soon developed sweating, thirst, and weakness; and the feeling of soreness spread to the left abdomen.

She was a non-clinic case; there had been no previous admissions. Her menstrual history was irrelevant except for menorrhagia. Her last normal period was in June. However, she had some bleeding during July and since had been spotting at intervals and passing clots.

Her blood pressure was 98/70, pulse 132, respiration 24, and temperature 100°. She was in distress with sweating, tachycardia, and grunting with a slightly accelerated respiration. Physical examination was negative excepting the abdomen and pelvis. A mass which was about 6 inches in diameter was noted just to the right of the umbilicus which extended into the right lumbar region. The patient had noted that the mass had developed since 2:00 p. m. the day of admission. Rigidity of the abdomen was more marked on the right side although there was some tenderness on the left. Dullness was present in both flanks and peristalsis was not heard. On vaginal examination a tender cervix was noted from which extended a thick chocolate discharge. The impression at that time was (1) ruptured ectopic pregnancy, (2) mild shock, (3) fluid in the abdomen, and (4) severe secondary anemia.

The white blood count was 21,500 with 92 per cent polymorphonuclears; 2,980,000 red cells; and 7 grams of hemoglobin; urine showed one plus albumin and glucose and 8-10 granular casts.

An exploratory laparotomy was performed under general anesthesia about two hours after admission. On opening the abdomen much blood was noted in the region of the cecum and ascending colon retroperitoneally. The tubes showed no evidence of pregnancy. It was decided to explore the accumulation of blood at the region of the cecum with the thought of a possible rupture of the kidney. On doing this, there was found in the region of the right kidney a fetus apparently two to three months of age. This was removed along with much blood and it was thought that it had been attached retroperitoneally. Bleeding was not controlled satisfactorily. Due to the condition of the patient and the inability to bring about satisfactory hemostasis, an attempt was made to control the bleeding by pressure packs which were brought to the outside of the abdomen through the incision thereby not completely closing the abdomen. The patient was in a critical condition. She was given 1500 c.c. of plasma, 900 c.c. of blood and 1000 c.c. of 5 per cent glucose while still on the table. Adrenalin, atropine, "coramine" were also administered. The patient expired at 6:00 a. m., approximately five hours after operation.

SUMMARY

(1) Three cases of abdominal pregnancy have been presented which were carried for nine months or longer on one obstetrical service within a period of one year.

(2) Abdominal pregnancy can be diagnosed with less difficulty if one suspects it in any case which "does not seem just right."

(3) X-rays are very valuable when used in advanced abdominal pregnancy, especially when a diagonal or other peculiar positions of the fetus is noted.

(4) If the fetus expires at or past the expected date of delivery without true labor or unusual symptoms, one should suspect abdominal pregnancy.

(5) Each of the cases presented showed some other disease or condition which may have been in some way responsible for the abdominal pregnancy. All were colored patients and came from a region where venereal disease is high.

(6) One infant was born alive but soon expired. This was probably due to congenital defects which are common in this condition.

(7) Alertness of the obstetrician and early diagnosis may save more infants. Leaving the placenta where it is, as in the three cases presented, may lower the high mortality from this rare form of pregnancy and save obstetricians a self-inflicted headache.

REFERENCES

1. Bard: Medical Obstetrics and Inq. London: **61**:1757, ii:369-372, 1762.
2. Baynham: N. Y. Medical and Phil. Rev., 1809.
3. King: Medical Repository. N. Y., 1817.
4. Swanson: J. Med. Soc. Michigan, **34**:585-589, 1935.
5. Mason: J. Obst. & Gyn., **39**:756-762, 1940.
6. Gardner and Middlebrook: Am. J. Surg., **66**:161-167, 1944.
7. Curtis: Obstetrics & Gynecology, iii:1937.
8. Meigs: Textbook of Obstetrics, 1849.
9. Nicodemus and Carrigg: J. Obst. & Gyn., **39**:153-154, 1940
10. Hudgins: W. Va. Med. Journal, **39**:277-282, 1943.
11. Ware and Maine: J. Obst. & Gyn., **27**:756-759, 1934.

BILATERAL MASTOIDITIS IN EIGHT WEEKS OLD BABY, JUNE 1945*

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Baby Jim B., 8 weeks old, full term, normal delivery, was brought to me. When this child was six weeks old the mother took him to her obstetrician for the routine six weeks check-up, and he was pronounced normal in every respect. A few days later she noticed a non-inflammatory swelling behind the right ear. There was no history of acute upper respiratory infection, severe earache, nor any specific reason to account for the swelling. She returned with the child to her physician and was advised to bring him back for further observation if the swelling did not disappear. Several days later a similar swelling appeared behind the left ear. At this time the baby had become restless, had a slight elevation of temperature. Several days later the child was referred to me for examination.

Other than a bilateral, inflammatory, fluctuating, swelling behind each ear over the region of the mastoid antra with elevation of temperature to 101° my examination was negative. There was a noticeable sagging of the posterior superior portion of each ear canal causing some narrowing of the lumen; the ear drums were intact and slightly thickened. The baby was sent to the hospital for operation.

Under the influence of a light ether anesthetic the usual incisions were made for performing an antrotomy on an infant. The cortex on each side had ruptured causing the release of pus under pressure. Culture showed streptococci. With the use of a curette the softened and ruptured plate of bone over the antrum of each ear was removed; excessive granulations were removed; the aditus ad antrum was located; the wound dusted with sulfanilamide powder; a rubber tissue drain inserted; two sutures were taken in the upper angle of the wound; and the usual dressing applied. The child made an uneventful recovery.

A perfectly normal infant, free of any respiratory infection with no evidence of middle ear infection insidiously developed a bilateral infection in the mastoid antra with findings the same on both sides.

June 12, 1945, Mrs. B. returned to my office with her daughter, Jean, aged 8. She gave the history that this child's left ear had been discharging for about four weeks, but that she was normal and healthy in every other way and had been attending school regularly.

Examination revealed a purulent discharge from the left middle ear. The drum was thickened and inflamed to the extent that all land marks were absent. There was an inflammatory, fluctuant swelling over the region of the mastoid antrum on the left side which had made its appearance several days previous to my examination. The remainder of the examination was essentially negative.

Under ether anesthesia the usual incisions were made. The cortex had ruptured in the region of the antrum. With the use of a curette the softened and ruptured plate of bone along with excessive granulations were removed. The process was well developed for a child of this age. Culture showed streptococci. I expect an uneventful recovery.

*Received for publication June 15, 1945.

PEPTIC ULCER AS A CAUSE OF ABDOMINAL SYMPTOMS IN CONGESTIVE HEART FAILURE*

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Practically all authors of textbooks of medicine describe the symptoms of abdominal distress frequently associated with heart failure. Heretofore, these symptoms have been uniformly ascribed to passive congestion in the viscera. Typical of the statements usually made is that by Christian in Osler's "Principles and Practice of Medicine":[1]

"Abdominal Distress.—Sometimes general, more often this is in the upper abdomen and especially in the right upper quadrant, where it is due to the distended liver, which may cause only a feeling of fulness or be tender and painful with all gradations between; as jaundice frequently occurs, not infrequently gallstones are considered the cause. Many of the cardiac patients have an uncomfortable full feeling in the epigastrium or generally over the abdomen which causes them to belch. Many have nausea, and vomiting is not infrequent * * * Stools may contain occult blood or even gross blood in considerable amount * * * all of these symptoms arise from chronic passive congestion."

In the light of the recent experience of the present authors, it would seem that a considerable proportion of the abdominal complaints of cardiac patients may be the result of a hitherto unsuspectedly high incidence of peptic ulcer among them.

During the first six months of 1944 at the Roper Hospital, two patients with congestive heart failure had such outspoken gastro-intestinal complaints that, although it was felt these were referable to heart failure, they were subjected to x-ray examination. Both proved to have easily demonstrable peptic ulcers. The first patient also had angina pectoris, and it was an interesting sequel that a Sippy diet caused the disappearance of what had been thought to be angina decubitus, although the angina of effort remained. The second patient had severe nausea and vomiting, which were not relieved by the discontinuance of digitalis. After Sippy therapy, the vomiting ceased and it was possible to digitalize him thoroughly, with marked improvement in the heart failure.

All patients with the diagnosis of peptic ulcer during the preceding six months were then reviewed, but none was found who had heart failure in addition. Moreover, a study of 50 consecutive autopsies on patients dying of congestive heart failure at Roper Hospital disclosed only two with peptic ulcer anatomically demonstrated. It was then determined for the next six months to x-ray all patients with heart disease and suggestive abdominal symptoms, and to ask the pathologist to pay particular attention to the upper gastrointestinal tract in patients dying with heart failure. Nine cases of peptic ulcer were demonstrated among cardiac patients during the latter period, interestingly enough, five of them by x-ray and four at autopsy.

We believe the probable reason why this relationship between cardiovascular disease and peptic ulcer has heretofore escaped attention is two-fold: the prevalence of passive congestion as an explanation for abdominal distress has discouraged x-ray study; and the pathologist in routine examination may overlook small ulcers or dismiss them as post-mortem digestion. At any rate, we have made the diagnosis much more frequently, both clinically and at autopsy, since our attention has been directed to the possibility.

It is not our purpose to enter into a discussion of the many theories of the pathogenesis of peptic ulcer. It is in the first place a very common disease, and we venture to predict that statistics will prove it to have an especially high incidence in patients with cardiovascular disease. Vascular factors have long been held important in its etiology, as summarized recently by Boles.[2]

It must be admitted that the clinical diagnosis of peptic ulcer in cardiac patients is difficult. Such factors as pain or distress from distended liver or congested and atonic viscera tend to mask and obscure the characteristic rhythm

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of ulcer distress, unless the symptoms are especially compelling as in our first two cases. Another confusing factor is that over-digitalization may result in a whole gamut of symptoms from anorexia to persistent nausea and vomiting. Even diuresis often produces gastrointestinal symptoms that have been attributed to mobilization of digitalis present in edema fluid. Accurate diagnosis will follow wider appreciation of the possibility of peptic ulcer in cardiac patients, and greater readiness to use x-ray investigation for their abdominal complaints, or at least to institute a therapeutic trial of frequent feedings.

SUMMARY OF CASES

Case 13469.—A 56-year-old white male, with hypertensive cardiovascular disease and anginal syndrome, had received digitalis two years. He developed severe epigastric pain and localized tenderness. X-ray showed duodenal ulcer. There was dramatic improvement of symptoms, including "angina decubitus," and disappearance of ulcer by x-ray following Sippy diet with recurrence of symptoms and x-ray findings three months later, again improved on diet.

Case 14264.—A 34-year-old Negro male, with syphilitic aortic insufficiency and hypertensive cardiovascular disease, and congestive failure for seven months, complained of epigastric discomfort, persistent nausea and vomiting, and diffuse epigastric tenderness, not relieved by discontinuing digitalis. X-ray showed duodenal ulcer. There was relief of symptoms with modified Sippy management. Repeat x-ray showed considerable healing.

Case 27346.—A 50-year-old Negro male, with hypertensive cardiovascular disease, and congestive failure for several weeks, developed massive gastrointestinal hemorrhage while under treatment for congestive failure, and died of exsanguination. Autopsy showed a perforating gastric ulcer with an eroded sclerotic artery at its base.

Case 16600.—A 27-year-old Negro woman, who suffered from hypertensive cardiovascular disease with malignant arteriolonephrosclerosis, had had congestive heart failure for several weeks. There were no abdominal complaints. Autopsy showed acute ulcerative esophagitis, gastritis and colitis.

Case 4389.—A 47-year-old Negro male, with hypertensive cardiovascular disease, had had mild congestive heart failure for several months. No symptoms or signs of peptic ulcer were recorded during life. Autopsy showed two small, acute gastric ulcers.

Case 30162.—A 60-year-old white man, with posterior coronary occlusion, developed congestive heart failure, epigastric pain, and persistent nausea and vomiting. X-ray showed duodenal ulcer. He improved on digitalis and frequent soft feedings.

Case 15828.—A 66-year-old Negro man, with hypertensive cardiovascular disease, had had congestive heart failure for two weeks. There were no gastrointestinal symptoms. Autopsy showed acute gastric ulcer of moderate size and depth.

Case 15809.—A 59-year-old Negro male, with arteriosclerotic heart disease, and congestive failure 18 months, complained of frequent epigastric fulness. X-ray showed duodenal ulcer, which improved under modified Sippy regime.

Case 6811.—A 32-year-old Negro woman, had hypertensive cardiovascular disease with congestive failure for two weeks. She complained of persistent epigastric fulness without relation to meals, and localized epigastric tenderness. Gastric analysis showed no free hydrochloric acid. X-ray showed duodenal ulcer. All gastric symptoms disappeared with modified Sippy regime.

Case 49952.—A 51-year-old Negro man, with hypertensive cardiovascular disease, and mild congestive failure for 18 months, complained of epigastric pain and localized tenderness 45 minutes after meals. X-ray showed pre-pyloric ulcer. He became symptom-free on dietary management.

Case 13647. — A 44-year-old Negro woman, with syphilitic aortic insufficiency, and aneurysm of the aorta, had congestive failure for 18 months. She complained of anorexia, flatulence, and minor epigastric tenderness. At autopsy an acute gastric ulcer and several smaller superficial erosions were seen.

Case 28744.—A 65-year-old Negro man, with syphilitic aortic insufficiency and hypertensive cardiovascular disease, had congestive failure for five months. He had no abdominal complaints during life. A penetrating gastric ulcer was found at autopsy.

A private case, a 61-year-old white man, had chronic myocardial insufficiency with auricular fibrillation, and mild congestive failure for two weeks. Gastrointestinal symptoms were denied. He was x-rayed because of suspicion of neoplastic involvement of the liver (irregular border), and a large duodenal ulcer crater was found. He was placed on a Sippy regime. The result is unknown.

From the summary of cases it will be seen that all patients in whom it was tried, received relief from ulcer management. In this connection, a word of caution may be mentioned: reasonable limits of food and fluid intake for the individual patient should not be exceeded. Moreover, a considerable increase in sodium intake will result if sodium bicarbonate is used as an antacid, and this may hinder the removal of edema. It is suggested that if frequent feedings do not give relief, non-sodium containing antacids should be employed.

SUMMARY

(1) Once attention was directed to the possibility, an unsuspected number of cases of peptic ulcer complicating heart failure were demonstrated, both by x-ray and at autopsy.

(2) It is suggested that many of the abdominal complaints in cardiovascular disease, heretofore explained on the basis of passive congestion, may really be due to a high incidence of acute or chronic peptic ulcer in these patients.

REFERENCES

1. Christian, H. A.: Osler's Principles and Practice of Medicine, 15th ed., p. 1018. New York: D. Appleton-Century Co., Inc.
2. Boles, R. S.: Frank Howard Lahey Birthday Volume, p. 85. Springfield, Illinois: Charles C. Thomas.

CAUSAL RELATIONSHIP BETWEEN OS CALCIS AND SHAPE OF LEG*

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The opinion is expressed frequently that Negroes have no well-developed calf muscles, a judgment based on the slimness of their legs. The conclusion is generally drawn that their legs are weaker than those of other races. However, the well-known fact that there are many Negro track athletes, and the remarkable records which some of them have achieved, should indicate the dubiousness of such a conclusion.

Actually Negroes very often have a longer os calcis than white people. In our X-Ray Department we see a considerable number of films taken of the feet of colored people, and sometimes the unusual length of the os calcis is quite striking. So far as the movement in the ankle joint is concerned, the longer Negro os calcis necessitates a mechanical adjustment in the muscles principally involved (gastrocnemius and soleus) which is different from the adjustment of a white person's. Consequently, whereas in white people a bulging calf is developed which gives the leg more or less of a bottle shape, in the Negro a long muscle is formed which gives his leg a stick-like appearance.

We by no means claim this as an original idea. That Negroes have as a rule a longer os calcis has been occasionally mentioned in anthropological literature, but the connection between that fact and the shape of the calf muscle has not been pointed out. Daniel G. Brinton[1] in *Races and People*, writes:

"The heel bone, the os calcis or calcaneum, is currently believed to be longer and project further backward in the Negro than in the white man. There is no doubt of the projection of the heel, and it is typical of the true Negro race, but it does not seem to be owing to the size of the bone, as an examination of a series of calcania in both races proves. The lengthening is apparent only and is due to the smallness of the calf and the slenderness of the main tendon, the tendon of Achilles, immediately above the heel."

Apparently cause and effect are reversed in this treatment of the subject. Although the true reason for the different muscle shapes is well known to most anatomists and biologists, it is usually stated only vaguely. Julian H. Lewis,[2] in *The Biology of the Negro*, says:

"The bones of the feet are said to vary in relation to race, especially the calcaneus, which is longer in the Negro, and accounts for the projecting heel in many colored people."

He does not discuss the connection between the slimness of the leg and the longer calcaneus, allowing the reader to assume that the shape of the leg and the length of the heel bone are entirely separate characteristics of the Negro race.

Others, like Hermann Braus[3] in his textbook on anatomy, and Richard Goldschmidt[4] in his book *Ascaris*, state the facts clearly, definitely pointing to the cause and effect relationship between the length of the os calcis and the shape of the calf muscles.

The foot is a two-armed lever, the main part of the foot forming the long anterior section of the lever, and the smaller part, the os calcis, forming the short posterior section. The ankle joint is the center of motion. Since the muscles coming down from the knee and attaching to the tuber calcanei pull the os calcis upwards by their contraction, the tip of the foot moves downward. Clearly, if the ratio of the anterior lever to the posterior lever is changed so that the center of motion is located farther toward the anterior end, the posterior tip of the heel bone has to be pulled upwards a greater distance in order to

*Received for publication April 30, 1945.
*From the X-Ray Department, Watts Hospital.

White: short os calcis, short, fleshy (strong) muscle belly, long tendon, pronounced calf.

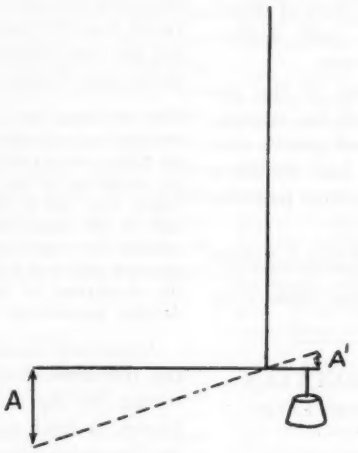
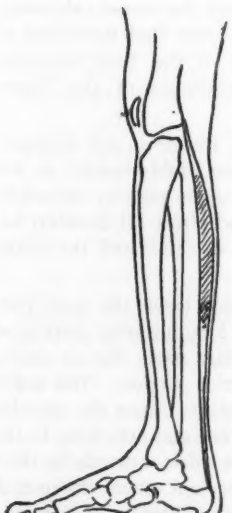


Fig. 1
Dist. A = A in Fig. 2. A^1 shorter than A^1 in Fig. 2.



Negro: long os calcis, long non-protruding muscle, short tendon, no calf.

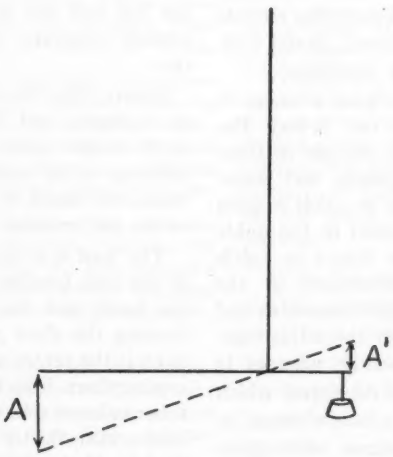


Fig. 2
Dist. A = A in Fig. 1. A^1 longer than in Fig. 1 because posterior lever is longer than in Fig. 1.

achieve an equivalent downward movement of the foot. Another consequence, according to the mechanical principles involved, is that in the latter case less power is needed.

The conditions just described are those of the skeleton of the Negro foot, in which the longer os calcis represents the longer posterior lever. The bones set the requirements; the muscles adjust themselves to those requirements. In the case of a longer os calcis, the muscles involved must be able to shorten to a greater extent when innervated. This adjustment is achieved by a longer muscle belly with only a short tendon. Any contraction of the muscle will then produce a greater shortening. That less strength is needed under these conditions is an additional reason for a thinner, fleshy muscle part.

We see, then, that the longer os calcis found in the Negro foot is the direct cause of a long and very slightly protruding muscle, which is responsible for the stick-like appearance of the calf that is apparent in so many Negroes. On the other hand, the skeleton of the foot in white people shows a short os calcis, or in other words a shorter posterior lever. The muscles involved have to be powerful but need to contract only over a short distance. This results in a muscle showing a long tendon and a short fleshy-muscle part which protrudes,

thereby causing the typical more or less inverted bottle shape of the calf in whites.

SUMMARY

(1) A particularly long os calcis in Negroes is a racial characteristic.

(2) This necessitates a different adjustment of the gastrocnemius and soleus muscles.

(3) The result is a non-protruding, slender calf in Negroes more or less stick-like in appearance in contrast to the protruding calf in white more or less bottle shaped.

REFERENCES

1. Brinton, Daniel G.: Races and People. Philadelphia: David MacKay, 1901.
2. Lewis, Julian H.: The Biology of the Negro. Chicago: Univ. of Chicago Press, 1942.
3. Braus, Hermann: Anatomie des Menschen. Berlin, Julius Springer, 1921.
4. Goldschmidt, Richard: Ascaris. Philadelphia: Prentiss Hall, Inc., 1937.

ERYSIPELAS ON THE ISTHMUS OF PANAMA*

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In a recent study of scarlet fever on the Isthmus of Panama during the forty-year period 1904-1944, it was found[1] that the incidence of the disease was low (2.7 cases per 10,000 Gorgas Hospital admissions) and that the diagnosis of scarlet fever was made five times more frequently in whites than in Negroes. Further investigation of the streptococcal diseases seemed desirable and hence a study of erysipelas was undertaken.

"Erysipelas is an acute localized inflammation of the skin and subcutaneous tissue, due to a streptococcus, and characterized by redness, edema, and induration, accompanied by systemic intoxication."[2]

During the forty-year period from May, 1904, to May, 1944, there were 540,760 admissions to Gorgas Hospital (known until 1927 as Ancon Hospital). A diagnosis of erysipelas was made on 369 occasions. Of these, 10 cases were rejected because the recorded data were grossly inadequate, 9 patients were transients, and 104 admissions represented recurrent attacks. The remaining 246 records fell into two groups. In 132 patients the recorded description of the skin lesions, even in the dark-skinned races, and the accompanying fever and malaise were so characteristic that the diagnosis of erysipelas could not be doubted. In the remaining 114 cases a final diagnosis of erysipelas had been made by the attending clinicians, but the recorded data did not permit adequate evaluation. These we designated by the term "erysipelas-like." The term "erysipeloid" was avoided because of the association of that term with swine erysipelas, a mild condition affecting primarily hands and fingers.[3] Bacteriologic studies were conducted in only a few cases. In our statistical studies no significant differences were found between the cases of erysipelas and erysipelas-like. For this reason we have presented the data on the entire group of 246 primary cases and, except where specified, the term erysipelas will be applied to the entire group.

Incidence, Annual and Seasonal Distribution.—The incidence of primary autochthonous erysipelas at Gorgas Hospital therefore was 4.6 per 10,000 admissions. (Total admissions to Gorgas Hospital include re-admissions.) Six patients, or 2.5 per cent died. No significant annual variation (*Table 1*) was noted during the forty-year period nor was there any significant difference in the incidence of the disease between the wet and dry seasons. (*Table 2.*)

Race, Sex, and Age Distribution.—The racial distribution of erysipelas with pertinent data on age, sex, and area of body involvement are recorded in *Tables 3, 4, and 5.*

In this paper the term race is used colloquially to designate a group of people distinctive in appearance, background, customs, and language. During the construction period of the Panama Canal a large number of Negroes were "imported" to the Canal Zone from the West Indies, mostly from Jamaica and Barbados. Although exact figures are not available, these Negroes and their families comprised 55 to 60 per cent

*Received for publication July 23, 1945.
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of the Gorgas Hospital population during the forty-year period under consideration. White United States citizens, mostly employees of the Canal, their families, or soldiers comprised 20 to 25 per cent. Ten per cent were mestizo Panamanians and 10 per cent a heterogeneous group. The incidence of the disease recorded in *Table 3* has been calculated on the assumption that whites constituted 25 per cent and Negroes 55 per cent of the hospital population, figures which underestimate the true difference. Males predominated in the hospital census in the ratio of 3 to 1.

Causative Factors. — Most authorities agree that erysipelas is initiated by an injury to the skin, often too minor to be noted by the patient. *Table 6* records the causative factors in those cases in which data were available. Nine patients specifically denied trauma and the remaining 126 charts contained no information on this point. In one case the illness followed a laceration with a machete while the patient was cutting orchids!

Symptoms.—In all cases local heat, redness, pain, and tenderness were present, as well as fever or some other systemic response such as malaise. Other symptoms mentioned on the

ANNUAL DISTRIBUTION

1904 (May-Dec.)	0	1925	6
1905	0	1926	3
1906	3	1927	8
1907	4	1928	12
1908	3	1929	11
1909	3	1930	19
1910	4	1931	12
1911	5	1932	8
1912	7	1933	6
1913	11	1934	8
1914	9	1935	3
1915	3	1936	9
1916	5	1937	5
1917	4	1938	9
1918	6	1939	3
1919	4	1940	3
1920	3	1941	9
1921	7	1942	5
1922	8	1943	7
1923	5	1944 (Jan.-May)	0
1924	6	Total	246

Table 1

SEASONAL DISTRIBUTION

Month	Number of Cases
January	20
February	26
March	19
April	20
May	26
June	20
July	15
August	20
September	20
October	20
November	22
December	18
Total	246

Table 2

RACIAL INCIDENCE

	U. S. White	W. Indian Negro	Panamanian Mestizos	Others	Total
Cases of Erysipelas	113	45	43	45	246
Incidence per 10,000 admissions (approximate)	8.2	1.8	7.8	8.2	4.6

Table 3

AGE AND SEX DISTRIBUTION ACCORDING TO RACE*

Age	U. S. White	West Indian Negro	Panamanian Mestizos	Others	Total
0-1	3 (1)	2	6 (3)	1 (1)	12
1-5	9	3	15	3	30
6-10	4	3	3	x	10
11-20	4	2	x	x	6
21-30	15	7	5	14	41
31-40	32	9	6	11	58
41-50	29	13 (1)	5	7	54
51-60	10	3	x	5	18
61-70	7	2	2	3	14
71-80	x	1	1	1	3
Total	113 (1)	45 (1)	43 (3)	45 (1)	246
Sex					
Males	84 (1)	25 (1)	12 (3)	30 (1)	151
Females	29	20	31	15	95

*Deaths in parentheses.

Table 4

charts are listed in the order of their frequency: chills 89; lymphadenitis, local 73; vomiting 43; headache 40; aching, generalized 27; nausea 22; anorexia 12; pharyngitis 8; cough 5; lymphadenitis, generalized 4; diarrhea 4; convulsions 4; icterus 3; distention 2; tremor 1; incontinence 1; delirium 1; photophobia, strabismus, and diplopia associated with orbital abscess 1; exhaustive toxic psychosis 1.

Laboratory Data.—At some time during their hospital stay 40 patients had some albumin in their urine and 10 of these had granular or hyaline casts. There were 2 cases of mild acute nephritis.

The leukocyte count varied from 3,650 in a 57-year-old United States male to 66,000 white cells per cu. mm. of blood in a 6-year-old Jamaican boy.

Severity of Disease and Complications.—An index of the severity of the illness is the temperature, initial and maximum readings of which are noted in *Table 7*. The duration of fever varied from 1 to 28 days; the mean was 5.1 days. Complications are listed in *Table 8*. Twenty-two complicated cases (8.9 per cent) correspond to the usual figure elsewhere before the advent of the sulfonamide drugs.[4,5] Two patients had recrudescences while still in the hospital. No significant racial differences in the severity of the disease or incidence of complications were found.

Recurrences.—There were 104 recurrences recorded in the charts examined, including 2 deaths. Of these, 36 were individual patients who had not had the primary or original attack treated in Gorgas Hospital. The remaining 68 represent subsequent admissions of patients already discussed in the main series; recurrences severe enough to require hospital entrance were not very different from primary attacks. However, as elsewhere, once the skin has been affected, recurrences may be quite frequent; 3 or 4 separate admissions with the complaint were not uncommon and how many minor transitory episodes received adequate home or dispensary care was impossible to determine.

Treatment.—The treatment in the earlier days was largely directed at relieving the local symptoms. Many received anti-streptococcus immunologic preparations. There were 32 patients treated with one or more of the sulfonamide drugs. In this small group two complications

AREA OF INVOLVEMENT ACCORDING TO RACE

Area	U. S. White	West Indian Negroes	Panamanian Mestizos	Others	Percentage of total (246 cases)
Head	27	17	7	9	24.4
Trunk	10	1	2	2	6.1
Upper Extremity	5	0	0	2	2.8
Lower Extremity	71	27	34	32	66.7
Total	113	45	43	45	100.

Table 5

CAUSATIVE FACTORS IN 111 CASES OF ERYSIPELAS

(1) Direct trauma	
Abrasions	19
Insect bites	15
Contusions	14
Lacerations	5
(2) Secondary to surgery	
Post-adenectomy	6
Burns	2
Compound fracture	1
Submucous resection	1
Antrotomy with removal of nasal spur	1
Frontal sinusotomy, bilateral	1
Tooth extraction	1
Circumcision	1
(3) Secondary to other disease	
Folliculitis	11
Ulcer, chronic	11
Furunculosis	3
Varicose veins	3
Lymphangitis, chronic	2
Trichophytosis, chronic	2
Tonsillar abscess	2
Varicella	2
Otomycosis	2
Otitis media, chronic, suppurative	1
Pansinusitis, suppurative	1
Herpes zoster	1
Impetigo contagiosa	1
Ulcer, acute	1
Arteriosclerosis	1
Total	111

Table 6

occurred; there were no fatalities. The average duration of fever in patients treated with sulfonamides was 4.1 days as compared to 5.2 days for the remainder, a reduction to be expected in view of recent reports.[4 6]

Deaths.—Eight patients died, 6 with primary, 2 with recurrent erysipelas. Their records are briefly summarized.

(1) A 6-month-old Panamanian male was admitted with erysipelas of both legs, vomiting, diarrhea, and fever. His white count was 39,600 per cu. mm. of blood. Autopsy (Dr. S. T. Darling) showed the cause of death to be erysipelas. Other anatomic diagnoses recorded were: enterocolitis, acute; bronchopneumonia; splenic hyperplasia; albuminuria.

(2) A 1½-year-old Greek child was admitted with erysipelas of the anterior and posterior portions of the thorax. He died shortly after admission. Pathologic diagnoses (Dr. H. C. Clark) included: erysipelas of thorax (listed as cause of death), gangrene of the skin of the external genitalia, acute purulent streptococcic peritonitis, acute purulent streptococcic meningitis.

(3) The patient was a 7-month-old Panamanian male who, following circumcision, developed streptococcic dermatitis and cellulitis of the legs, thighs, and genital region. He had a bacteremia with streptococcic effusions to the serous cavities, bilateral acute otitis media, bronchopneumonia, and streptococcic furuncles of the scalp. The cause of death was recorded as erysipelas (Dr. F. F. Russell).

(4) Following trauma to his scrotum, a 46-year-old French West Indian developed dermatitis and gangrene of that area, requiring surgical intervention. A blood culture taken on the day preceding his death was sterile. Autopsy (Dr. H. C. Clark) showed he had acute streptococcic dermatitis and cellulitis of the external genitalia, lower abdomen, and inner surface of the thighs, and local lymphadenitis.

(5) A 4-month-old United States white male was admitted because of bilateral otitis media, acute, suppurative (organism not stated). Erysipelas was present over the posterior thorax on admission and continued to spread. On the eighteenth hospital day a left mastoidectomy was done but the baby continued to fail. The cause of death was recorded as "infantile erysipelas" complicated by suppurative otitis media, bilateral. No autopsy was done.

(6) A 2-month-old Panamanian male entered with erysipelas of the face so severe as to prevent opening the eyes. The white cell count was 13,100 per cu. mm.; albumin and casts were present in the urine. The scalp became affected; septicemia developed, and he succumbed 22 days after entry. Anatomic diagnoses at autopsy (Dr. R. O. Dart) included erysipelas of the face, multiple abscesses of the scalp, streptococcic septicemia, bronchopneumonia, catarrhal otitis media, central focal liver necrosis, and jaundice.

The following two patients died with recurrent erysipelas:

(1) An 86-year-old Jewish male resident of the Canal Zone had had erysipelas 16 years before. He entered with senile gangrene of his right leg and a complicating erysipelas of the adjacent skin; he expired on his fourth hospital day. No autopsy was permitted.

(2) After many admissions for recurrent erysipelas this 34-year-old United States white woman came to Gorgas Hospital with erysipelas which first involved the left upper extremity and then the thorax. A blood stream infection developed and she died on the third hospital day. Autopsy (Dr. R. O. Dart) showed that erysipelas complicated by a streptococcic septicemia was the cause of death.

DISTRIBUTION OF ADMISSION AND MAXIMUM TEMPERATURE READINGS

Degrees of Temperature	Admission Temperature (Number of Cases)	Maximum Temperature (Number of Cases)
97-98	1	0
98-99	26	6
99-100	35	14
100-101	32	26
101-102	36	24
102-103	47	43
103-104	39	51
104-105	23	54
105-106	7	24
106-107	0	4
Total	246	246

Table 7

COMPLICATIONS: NON-FATAL AND FATAL CASES

(1) Complications with recovery (16 cases)	
Vesiculation	5
Abscess	3
Folliculitis	2
Nephritis, acute, mild	2
Bronchopneumonia	1
Septicemia	1
Exhaustive psychosis	1
Ulceration and slough, nose	1
(2) Fatal complications (5 cases)	
Bronchopneumonia	3
Otitis media, acute, bilateral	3
Abscess of affected area	2
Gangrene of affected area	2
Peritonitis	2
Meningitis	1
Purulent serositis	1
Nephritis, acute, severe	1
Enterocolitis, acute	1

Table 8

Discussion.—The striking feature of the foregoing data is the racial difference in the incidence of erysipelas. In the study of scarlet fever on the Isthmus it was found that the diagnosis was made five times more frequently in whites than in Negroes. Because of the difficulty of making a diagnosis of a mild case of scarlet fever in Negroes some doubt might be entertained as to the veracity of these figures. On the Canal Zone free hospitalization is provided for employees and there is no loss of pay for short illnesses. Charges for families of employees are minimal. There is no reason to believe, therefore, that Negroes with erysipelas would not seek medical treatment as often as whites, when they seek such attention for other diseases. Hence the fact that the diagnosis of erysipelas was made four to five times more frequently in whites than in Negroes seems significant. Holmes[7] wrote:

"Erysipelas, like other streptococcus diseases is relatively infrequent among Negroes and causes much fewer deaths in infancy than among the whites, notwithstanding the unhygienic conditions commonly surrounding the Negro child."

He attributed the racial differences to the "resistant ectoderm" of the Negro.[8] (See Lewis[9] for summary of the literature.)

Erysipelas as it occurs on the Isthmus is essentially similar in its clinical manifestations, course, complications, and mortality to the disease in temperate climates if certain local factors are taken into consideration. The location of 70 per cent of the lesions on the lower extremity in comparison with 90 per cent facial involvement in the United States[2] can be explained by the frequency of trauma in a population much of which is engaged in excavation and construction. The high young adult population on the Isthmus also explains the age distribution of the cases. The large number of cases in females, as was also true of scarlet fever,[1] defies explanation.

SUMMARY

(1) During the forty-year period 1904-1944 there were 246 individuals with primary autochthonous erysipelas admitted to Gorgas Hospital, Canal Zone. The rate was 4.6 per 10,000 hospital admissions. Six patients or 2.5 per cent died.

(2) No significant seasonal or annual variations in incidence were noted.

(3) The disease was primarily one of adult life, 62.2 per cent of all cases being between 21 and 50 years of age. The lesions involved the extremities in 69.5 per cent, the head in only 24.4 per cent of the patients. In 8.9 per cent complications occurred.

(4) A distinct racial variation was noted. United States white patients had an incidence of 8.2 per 10,000 hospital admissions, Panamanian mestizos 7.8, and West Indian Negroes only 1.8 per 10,000 admissions. These data corroborate the generally accepted opinion that the Negro has a remarkable resistance to erysipelas.

BIBLIOGRAPHY

1. Tucker, H. A.; Miller, W. C.; and Kean, B. H.: Scarlet Fever on the Isthmus of Panama. Sou. Med. Jour., **38**:761 (November) 1945.
2. Sutton, R. L.; and Sutton, R. L., Jr.: Diseases of the Skin, Ed. 10, p. 896. St. Louis: The C. V. Mosby Company, 1939.
3. Becker, S. W.; and Obermayer, M. E.: Modern Dermatology and Syphilology, p. 323. Philadelphia: J. B. Lippincott Company, 1940.
4. Shank, R. E.; Maxwell, R. W.; and Bozalis, R. S.: Sulfonamides in the Treatment of Erysipelas. J.A.M.A., **117**: 2238-2239 (Dec.) 1941.
5. Dawson, M. H.: Erysipelas. In Cecil, R. L.: A Textbook of Medicine by American Authors, ed. 6, pp. 143-145. Philadelphia: W. B. Saunders Company, 1943.
6. Bruce, J. W.; and Chalkley, T. S.: Erysipelas in Infancy. Am. J. Dis. Child., **65**:739-743 (May) 1943.
7. Holmes, S. J.: Differential Mortality in the American Negro. Human Biol., **3**:71-106, 1931.
8. Holmes, S. J.: The Resistant Ectoderm of the Negro. Am. J. Phys. Anthrop., **12**:139-153 (July-Sept.) 1928-1929.
9. Lewis, J. H.: The Biology of the Negro, p. 382. Chicago: University of Chicago Press, 1942.

SCARLET FEVER ON THE ISTHMUS OF PANAMA*

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The geographic and anthropathologic** distribution of the streptococcal diseases is of such widespread interest that it seemed worthwhile to present the available data on scarlet fever, a disease which is universally regarded as being caused by the hemolytic streptococcus. The only previous local report with which we are

*Received for publication July 23, 1945.

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**Anthropathology is a term recently introduced by Lewis[9] meaning comparative racial pathology.

acquainted was furnished by Levy[2] who summarized 10 cases from the Canal Zone in 1914. His cases are included in the present study.

Helmholz[3] defined scarlet fever as "an acute infectious disease caused by the *Streptococcus scarlatinae*, and characterized by a sore throat and a punctate rash on the skin and roof of the mouth, followed by desquamation." Not all patients show all of the characteristics of the disease. The rash may be especially difficult to recognize in dark-skinned people. For inclusion of a case in this series we required that: (1) the attending physician make the diagnosis of scarlet fever, (2) the patient show systemic signs, such as fever, leukocytosis, rash, or lymphadenopathy, (3) and, in questionable cases, desquamation occur.

During the forty-year period from May 1904 to May 1944, in 540,760 admissions to Gorgas Hospital (formerly Ancon Hospital), Canal Zone, diagnoses of scarlet fever were made in 174 cases. Of these, 20 patients were transients who arrived on the Isthmus of Panama with scarlet fever or who developed the disease within the incubation period. Eight cases were rejected because they did not meet our criteria for the diagnosis of scarlet fever. The remaining 146 cases provided the data for this report. There were no recurrences of the disease. The incidence of scarlet fever was 2.7 per 10,000 hospital admissions. (Many admissions to Gorgas Hospital represent readmissions of the same patient.) Four patients died, so the mortality rate was 2.7 per cent.

Annual and Seasonal Distribution.—The annual distribution of cases of scarlet fever is recorded in *Table 1*. The seasonal distribution is indicated in *Table 2*. The wet season on the Isthmus, in general, extends from May through December, and the dry season from January through April. Of the 36 cases in 1921, 30 occurred in the six months' period from March through August. The patients represented all race groups and came primarily from the large terminal communities on the Atlantic and Pacific sides of the Isthmus.

Age.—As elsewhere, the disease on the Isthmus of Panama is one of childhood. Seventy-nine and one-half per cent of the patients were under 16 years of age, 66.4 per cent 10 years or less, and 28.8 per cent 5 years or less (*Graph 1*). The population of the Canal Zone has been predominately young adult male.

Race and Sex.—As is shown in *Table 3*, there were well over twice as many cases in whites as in Negroes. Exact figures are not available, but approximately 55 to 60 per cent of the

ANNUAL DISTRIBUTION 1904-1944

1904 (May)	0	1925	0
1905	0	1926	0
1906	0	1927	2
1907	0	1928	2
1908	0	1929	2
1909	4	1930	2
1910	3	1931	9
1911	0	1932	9
1912	1	1933	4
1913	6	1934	3
1914	4	1935	2
1915	1	1936	1
1916	0	1937	7
1917	2	1938	7
1918	0	1939	3
1919	1	1940	2
1920	7	1941	2
1921	36	1942	0
1922	9	1943	8
1923	4	1944 (May)	0
1924	3		—
		Total	146

Table 1

SEASONAL DISTRIBUTION 1904-1944 AND IN 1921

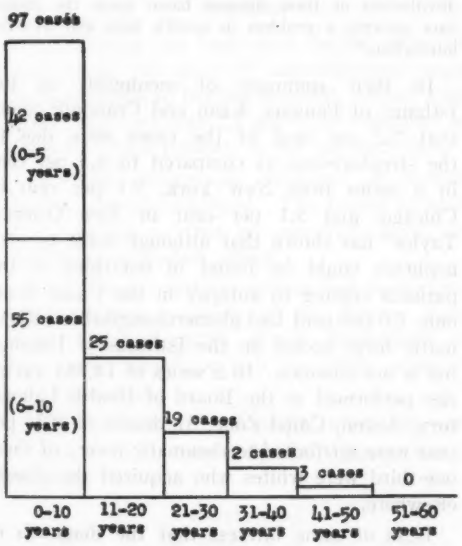
Month	1904-1944	1921
January	12	0
February	14	2
March	17	7
April	11	5
May	16	4
June	9	1
July	15	6
August	15	7
September	3	0
October	10	1
November	9	1
December	15	2
	—	—
Totals	146	36

Table 2

Gorgas Hospital population during the period under consideration were Negroes (mostly British West Indians "imported" for the construction of the Panama Canal), 20 to 25 per cent were white Americans, 10 per cent were mestizo Panamanians, and 10 per cent a heterogeneous group composed mainly of adult transient seamen and laborers. The incidences of the disease recorded in *Table 3* have been calculated on the assumption that Negroes constituted 55 per cent and whites 25 per cent of the hospital population, figures which underestimate the true difference. A diagnosis of scarlet fever, therefore, was made at least five times more frequently in whites than in Negroes.

No explanation for the high percentage of females in our series is forthcoming. In the general hospital population there were at least 3 males to 1 female, but in children age 10 years and under the ratio was 1½ males to 1 female.

Symptoms.—Fever, sore throat, and desquamation occurred in nearly all cases. The exanthem was almost universal in whites. The following particular symptoms were recorded: cervical adenitis 67; vomiting 56; tonsillitis, severe 37; headache 28; cough 20; joint pains 16; anorexia 14; generalized adenitis 11; abdominal pain 10; nausea 9; chills 5; delirium 4; convulsions 2; prostration 2; conjunctivitis 2; splenomegaly 2; constipation 1; vertigo 1; icterus 1.



Graph 1
Age distribution by decades of 146 cases of scarlet fever.

Laboratory Data.—In 44 cases there was albumin in the urine at least once during the hospital stay; in 28, hyaline or granular casts were found. The remaining cases had no apparent kidney involvement as shown by the laboratory reports.

Leukocytosis was the rule. White cell counts varied from 4,400 to 28,650 per cu. mm. of blood, the average for the group being 14,250 per cu. mm.

Severity of Disease and Complications.—The severity of the disease may be judged by *Table 4* which records temperature data. The following complications occurred: cervical adenitis, severe 15; arthritis 6; nephritis 5; otitis media, bilateral 4; tonsillitis, severe 2; myocarditis 2;

RACE AND SEX DISTRIBUTION

	U. S. White	West Indian Negroes	Panamanian Mestizos	Others	Total
Males	29	10	16	4	59
Females	40	19	21	7	87
Total	69	29	37	11	146
Incidence (approximate)	5.0 per 10,000 admissions	1.0 per 10,000 admissions	6.7 per 10,000 admissions	2.0 per 10,000 admissions	2.7 per 10,000 admissions

Table 3

ADMISSION AND MAXIMUM TEMPERATURE READINGS

Temperature (Degrees F.)	On Admission	Maximum
98-99	1	1
99-100	16	7
100-101	34	19
101-102	29	18
102-103	38	33
103-104	13	31
104-105	12	32
Over 105	3	5
	146	146

Table 4

impetigo 2; vesiculation 1; phlegmonous pharyngitis 1; bronchopneumonia 1; septicemia 1; rhinitis 1; conjunctivitis 1; ecthyma 1; paronychia 1.

The following concomitant diseases were listed: measles 11; malaria 1; varicella 1; herpes zoster 1; Vincent's angina 1; diphtheria 1.

Treatment.—Fifteen of the patients received one or more of the sulfonamide drugs; the remainder received antitoxins or merely symptomatic therapy. None of the patients who died received any of the sulfonamide preparations.

Deaths.—Four patients died. Their records are summarized briefly.

(1) A 3-year-old Jamaican Negro female entered the hospital with circumoral pallor, rash, fever, sore throat, splenomegaly, and signs of pleuritis. Throat cultures were positive for *Streptococcus hemolyticus*. She expired on her second hospital day. Autopsy (Dr. H. C. Clark) disclosed acute ulcerative tonsillitis, general lymphadenitis, and acute enlargement of the spleen with subcapsular hemorrhage.

(2) A 7-year-old Barbadian Negro male was admitted with severe scarlet fever and marked tonsillar involvement. He died on the third hospital day. Autopsy (Dr. H. C. Clark) showed a bacteremia (*Streptococcus hemolyticus*) with lymphadenitis, purulent arthritis, sinusitis, icterus, and extreme parenchymatous degeneration of kidneys, heart, and liver.

(3) An 8-year-old United States white girl had scarlet fever with marked throat symptoms. A membrane involving the nose, throat, and larynx necessitated an emergency tracheotomy six days after entry. Autopsy (Dr. E. DeCoursey) showed phlegmonous laryngitis and pharyngitis with laryngeal stenosis, bronchopneumonia, acute suppurative lymphadenitis, focal necrosis of liver and adrenals, and acute splenic tumor.

(4) A 5-year-old Panamanian girl had had a sore throat and fever two weeks prior to entry. Chief complaints on admission were edema, dark-colored, scanty urine, pain in the kidney regions, and desquamation of the arms and legs. The white cell count was 24,600 per cu. mm. of blood; the urine contained albumin and casts. Bronchopneumonia complicated the course and she expired on her seventh hospital day. The cause of death clinically was considered to be postscarlatinal nephritis with secondary anasarca and bronchopneumonia. The autopsy (Dr. H. W. Mahon) confirmed the clinical diagnoses and in addition showed cardiac hypertrophy, pulmonary edema, and generalized lymphadenopathy.

Discussion.—In the most recent edition of Cecil's Textbook of Medicine[3] is the following statement about scarlet fever: "The disease is practically unknown in the tropics." This exaggeration expresses the generally held view that the morbidity and mortality of scarlet fever and some other streptococcal diseases are markedly less in tropical than in temperate areas. The latitude of Panama is 8 degrees North. The temperature tends to be uniform, rarely varying from the range of 65 to 95° F. A four months' dry season and eight months' wet season is the rule. The incidence of scarlet fever in this region is indeed low: 2.7 cases per 10,000 hospital admissions. The course of the disease is essentially similar to that in more temperate zones, although it is possible that the disease is somewhat milder.

Other investigators have demonstrated that the incidence of scarlet fever and other streptococcic diseases is less in tropical than in temperate areas. Seegal, Seegal and Jost,[4] for example, reported that in North America the rate for scarlet fever and rheumatic fever "diminishes progressively from latitude 50-45 degrees to 34-29 degrees" but that the "rate for glomerulonephritis does not vary significantly in the four latitude regions studied." They wrote:

"Since evidence is available ascribing etiologic significance to the hemolytic streptococcus in all three diseases studied here, the variations in the geographic distribution of these diseases based upon the limited data presents a problem in specific host and bacterial interaction."

In their summary of meningitis on the Isthmus of Panama, Kean and Crandall[5] found that 7.2 per cent of the cases were due to the streptococcus as compared to 8.5 per cent in a series from New York, 9.1 per cent in Chicago, and 5.1 per cent in New Orleans. Taylor[6] has shown that although some type of nephritis could be found in one-third of the patients coming to autopsy in the Canal Zone, only 1.0 per cent had glomerulonephritis. Rheumatic fever occurs on the Isthmus of Panama, but is not common. In a series of 14,381 autopsies performed at the Board of Health Laboratory, Ancon, Canal Zone, 37 deaths or 0.27 per cent were attributed to rheumatic fever; of these one-third were whites who acquired the disease elsewhere.

It is of some interest that the diagnosis of scarlet fever was made five times more frequently in whites than in Negroes. These figures

are in agreement with the statistics presented by Holmes.[7 8] The apparent preponderance of cases in whites may be due to the difficulty of diagnosis in Negroes. Desquamation, however, is so definite a sign that not many hospitalized cases are overlooked. It is of course possible that the rash which is well recognized by the laity brings white patients to the hospital more frequently than Negroes.

The theory that Negroes are less susceptible to the disease has been extensively discussed. (See Lewis[9] for summary of literature.) Doull,[10] for example, says that although it is probably true that attacks of scarlet fever are frequently overlooked in the Negro this "cannot account for mortality differences which are so conspicuously and consistently in favor of the Negro." Cornely,[11] on the other hand, has presented evidence controverting statistics purporting to show that the mortality and morbidity of scarlet fever is higher in Southern whites than in Southern Negroes. Holmes[7 8] believes that the "resistant ectoderm" of the skin and oropharynx of the Negro is responsible for the difference in the incidence of some streptococcal diseases in Negroes and white, while Doull[10] attributes the difference to the longer racial experience of the Negro race.

SUMMARY

(1) During the forty-year period 1904-1944 there were 146 cases of autochthonous scarlet fever admitted to Gorgas Hospital, Ancon, Canal Zone. The rate was 2.7 per 10,000 hospital admissions. Four patients or 2.7 per cent died.

(2) The disease, as elsewhere, is predominantly one of childhood. The course is essentially similar to that in temperate zones, but it may be somewhat milder.

(3) The wet and dry seasons had no apparent effect on the incidence of the disease. Cases were scattered rather evenly throughout the forty-year period except for 1921, when 36 cases occurred.

(4) The diagnosis of scarlet fever was made 5 times more frequently in whites than in Negroes.

REFERENCES

1. Lewis, J. H.: The Biology of the Negro, preface, p. X. Chicago: University of Chicago Press, 1942.
2. Levy, W. V.: Scarlet Fever on the Canal Zone. Proc. Med. Assn. Isthmian Canal Zone, 7, (part II) 25-31 (Nov.) 1914.
3. Helmholz, H. F.: Scarlet Fever. In Cecil, R. L.: A Textbook of Medicine by American Authors. Ed. 6, pp. 145-155. Philadelphia: W. B. Saunders Company, 1943.
4. Seegal, D.; Seegal, E.B.C.; and Jost, E. L.: A Comparative Study of the Geographic Distribution of Rheumatic Fever, Scarlet Fever and Acute Glomerulonephritis in North America. Amer. J. Med. Sci., **190**:383-389 (Sept.) 1935.
5. Kean, B. H.; and Crandall, W. D.: Meningitis on the Isthmus of Panama. Am. J. Trop. Med., **24**:17-23 (Jan.) 1944.
6. Taylor, C. E.: The Racial Incidence of Nephritis and Hypertension in Panama. To be published.
7. Holmes, S. J.: The Resistant Ectoderm of the Negro. Am. J. Phys. Anthrop., **12**:139-153, (July-Sept.) 1928-1929.
8. Holmes, S. J.: Differential Mortality in the American Negro. Human Biol., **3**:71-106, 1931.
9. Doull, J. A.: Comparative Racial Immunity to Diseases. J. Negro Education, VI, 3, 429-437 (July) 1937.
10. Lewis, J. H.: Reference No. 1, pp. 207-210.
11. Cornely, P. B.: Morbidity and Mortality from Scarlet Fever in the Negro. Am. J. Pub. Health, **29**:999-1005 (Sept.) 1939.

ACUTE BACTERIAL ENDOCARDITIS IN A DRUG ADDICT*

A CASE REPORT

By EDWARD T. BRADING, M.D.
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Recently Hussey and others[1] reported five cases of septicemia and bacterial endocarditis resulting from heroin addiction. The following case report is of interest as an addition to their series of cases and because it involved a practicing physician.

E. M., a practicing physician in a neighboring rural community, was admitted to the Appalachian Hospital on September 3, 1944, because of chills and fever of two weeks' duration. The patient, although an active practitioner, had been a known narcotic addict for several years. The authorities had revoked his narcotic license and he was compelled to boil down tincture of camphorated opium to supplement an inadequate and uncertain supply of morphine and pantopon. He injected the drugs intravenously.

For two weeks prior to admission he had noticed increasing malaise associated with afternoon temperature and night sweats. Despite this he continued working until three days prior to admission when his strength became so impaired and symptoms so severe that he was compelled to go to bed.

On admission to the hospital, examination revealed a well developed and nourished man, 47 years of age who looked older than his stated age and who was evidently acutely ill. On admission his temperature was 103°, pulse 105. His mouth and throat were clear. There were scattered, moderately coarse rales heard over the right lung posteriorly. The heart was normal in size to percussion. Blood pressure was 130/85. No abnormal sounds were heard in the heart. The spleen was not

*Received for publication April 6, 1945.

felt. The abdomen was moderately distended, tympanitic throughout. The liver edge was felt about two centimeters below the costal margin. It was distinct and not tender. There were numerous scars over the veins of both arms and much subcutaneous induration; so much that none of the arm veins could be used and during his entire illness resort was made to the veins in the ankles for the taking of specimens and giving of transfusions and fluids. X-ray of the chest, taken on admission, showed several cottony shadows scattered through both lungs but more obvious on the right, which were thought by the x-ray department to be conglomerated tubercles. Hemoglobin was fifteen grams; red blood cells 5,100,000, white blood cells 16,800. Differential count showed polymorphonuclears 82 per cent and lymphocytes 18 per cent. Blood culture was negative. Agglutinations for tularemia, malta fever, brucellosis, typhoid and paratyphoid were all negative. Cultures of stools and urine were negative. Blood cultures on two successive days were reported negative. During the first week of the hospitalization he was given sulfadiazine, approximately 160 grams daily for five days without any improvement. One week after admission an x-ray of the chest showed no material changes in the previous picture, but physical examination of the chest disclosed scattered, moderately coarse rales at this time and there appeared for the first time a soft systolic murmur heard best in the mid-sternum and along the left border of the sternum at the attachment of the fourth rib. At this time he was started on large doses of penicillin (250,000 units daily), but despite this and numerous transfusions, the course of the disorder was progressively downward. On the fourteenth day an x-ray of the chest showed a mottled density scattered through portions of both lungs. The x-ray had the appearance of multiple abscesses and in the right pleural cavity there was a small amount of fluid, a portion of which was aspirated for diagnosis. In this fluid Staphylococcus aureus was found and on this day for the first time there was reported a positive blood culture of Staphylococcus. The heart murmur became somewhat more evident but was never loud or prolonged. The patient expired on the sixteenth day after admission.

The clinical diagnosis was multiple metastatic abscesses of the lung, probably from bacterial endocarditis. A post-mortem examination showed a vegetative endocarditis of the tricuspid valve with multiple metastatic abscesses scattered throughout both lungs.

REFERENCE

1. Hussey, H. H.; Kelliher, T. F.; Schaefer, B. F.; and Walsh, B. J.: Septicemia and Bacterial Endocarditis Resulting from Heroin Addiction. J.A.M.A., **126**:535 (Oct. 28) 1944.

505 Hamilton Bank Building

Southern Medical Journal

JOURNAL OF THE

SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1945. Published monthly by the Southern Medical Association, Empire Building, Birmingham 3, Alabama. Annual subscription, $4.00. Single copies 35c each.

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Volume 38 NOVEMBER 1945 Number 11

EDITORIAL DEPARTMENT

VICTORY MEETING IN CINCINNATI
November 12 through 15

Plans are now practically complete for the thirty-ninth annual meeting of the Southern Medical Association, which convenes upon the invitation of the Campbell-Kenton County Medical Society of Kentucky. The final printing of the program has been delayed, but it is hoped that programs may be mailed to members of the Association before the opening convention date. Every effort has been made to include all regular peacetime activities of the Association, giving each its usual place and importance. Social activities will be resumed. The meeting opens at noon on Monday, November 12, programs beginning at 2:00 p. m.

Problems of the war just past, of reconversion, and of the people and the medical profession in civil life will be discussed as well as the directions of the generally rapid trend of medical progress in wartime. During the past five years scientific methods and technics have advanced almost as fast as munitions and armament manufacture, while up to now physicians have had little time for general evaluation of them. An opportunity for large scale discussion is now at hand.

An unusually meaty program is now being completed. A glance through the programs as already turned in shows many interesting and arresting titles. There will be found work upon current aspects of the sociologic side of medicine, the effects of increasing development of hospitalization, rural medical care, demobilization, and rehabilitation of members of the armed forces. Deficiency diseases in this country and in Germany, German medical schools during the occupation, uses of penicillin and comparison of its *in vitro* and *in vivo* effects, progress in cardiology and circulatory disturbances, congenital heart diseases, sources of dyspepsia and gastro-intestinal pain, sulfonamides in infectious diseases of the bowels, and hemostasis in neurosurgery are covered. There will be reports upon psychotherapy of schizophrenia, and of the menopause, effects of promin upon leprosy, newer developments in dermatophytosis, pregnancy tests, kidney and ureter surgery and diagnosis, surgical treatment of war deformities, a demonstration of mass venereal disease control in a southern city, and discussion of the development of new medical schools in the South. Speakers will be among the ablest men in the country, and convention guests will find it difficult to choose which of many interesting concurrent sessions to attend.

Cincinnati is a great city, both in its present and its past. Founded soon after the American Revolution, it has grown with the middle west as a center of business, culture, and education. It is well worth a visit for its own intrinsic interest.

MACROCYTIC ANEMIA

The value of liver in the treatment of pernicious anemia was first conclusively demonstrated by Minot and Murphy in 1926.[1] Three years later Sharp showed that desiccated hog stomach is also an effective remedy in this disease.[2] Mammalian kidney[3] and brain,[4] brewers' yeast,[5] and other substances have been shown to possess anti-anemic material.

1. Minot, G. R.; and Murphy, W. P.: Treatment of Pernicious Anemia by a Special Diet. J.A.M.A., **87**:470, 1926.
2. Sharp, E. A.: An Anti-anemic Factor in Desiccated Stomach. J.A.M.A., **93**:749, 1929.
3. McCann, W. S.: Effect of Kidney on Blood Regeneration in Pernicious Anemia. Proc. Soc. Exper. Biol. and Med., **25**: 255, 1928.
4. Ungley, C. C.: Effect of Brain Diet in Subacute Combined Degeneration of Cord. Lancet, **1**:227, 1932.
5. Wintrobe, M. M.: The Anti-anemic Effect of Yeast in Pernicious Anemia. Amer. J. Med. Sci., **197**:286, 1939.

Castle[6] has demonstrated that the gastric juice from a normal person when incubated with beef and fed to a person with addisonian pernicious anemia in relapse will produce a remission in the patient, whereas the gastric juice from a person with addisonian pernicious anemia when incubated similarly with beef and fed to a patient in relapse will not produce a remission. Castle thus concluded that there is an underlying defect in the gastric secretion of persons with pernicious anemia. He termed this the "intrinsic factor." The "extrinsic factor" is present in foods, and it is thought that beef muscle, rice polishings, and other substances contain this "extrinsic factor," which requires incubation with the gastric juice from another person in order to remit a patient with pernicious anemia.

Macrocytic anemia occurs not only as the addisonian "pernicious" variety, commonly considered an entity, but also with liver disease, pregnancy, sprue, and with pellagra. Definition of these types on etiologic grounds and according to Castle's formula has been logical but theoretical and not entirely satisfactory. With the isolation, synthesis, and clinical testing of pure substances, however, which are potent in the regeneration of the blood, physicians may expect a better understanding of the pathogenesis of each of these special types.

Spies and Payne,[7] while studying the etiological relationship between macrocytic anemia in pellagrins and pernicious anemia, showed that the gastric juice from such patients with pellagra when incubated with ground beef would cause remission of symptoms of typical pernicious anemia.

Another milestone in the study of macrocytic anemias is described in the current issue of the Journal. Spies, Vilter, Koch, and Caldwell[8] have shown that synthetic folic acid when given either parenterally or orally is followed by a sharp increase in the reticulocytes and a subsequent increase in the total red blood cell counts and the hemoglobin content of the peripheral blood. The authors regard this substance as a part of the vitamin B group, and they make no claims that it produces all the results that follow the administration of potent liver extract.

During the past decade there have been many attempts to find a single synthetic chemical substance which would produce the type of rise described in this paper. Each of these attempts has failed. The knowledge that a single chemical factor will produce such a change will enable scientists to evaluate better the exact nature and relationship of the anti-anemic substances in foods. Many other factors will have to be isolated, identified, and tested before full information is available.

6. Castle, W. B.; and Townsend, W. C.: Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: II. Effect of Administration to Patients with Pernicious Anemia of Beef Muscle After Incubation with Normal Human Gastric Juice. Am. Jour. Med. Sci., **178**:764, 1929.

7. Spies, T. D.; and Payne, W. A.: A Study of the Etiological Relationship Between Pellagra and Pernicious Anemia. Jour. Clin. Invest., **12**:229, 1933.

8. Spies, T. D.; Vilter, Carl F.; Caldwell, Margaret H.; Koch, Mary B.: Observations on the Anti-anemic Properties of Synthetic Folic Acid. Sou. Med. Jour., p. 707, this issue.

TREATMENT OF PELLAGRA AND NUTRITIONAL EDEMA IN INFANTS

Many types of deficiency disease are to be expected in the war scarred world this winter, and their treatment in advanced stages assumes an ever increasing interest. The Union of South Africa has not been a battlefield. However, its medical school in Johannesburg reports prevalence of deficiency disease among non-European children, in particular of a severe syndrome provisionally called pellagra, with a death rate of around fifty per cent. The infants show, among other symptoms, severe edema and steatorrhea; and by numerous biopsy studies of the liver, Gillman and Gillman[1] have demonstrated that this organ is invariably damaged very early, with an abnormal accumulation of fat. The typical cutaneous lesions occurred: labial and angular stomatitis, glossitis, a peculiar depigmentation of the skin over the entire body, and a graying of the hair of the scalp with varying degrees of alopecia. The tongue was not raw, red and beefy as in adult pellagra, but smooth and atrophic. Vitamins were of no benefit in the condition, and the prognosis was largely determined by the severity of the hepatic injury. The fatty liver these authors consider the most

1. Gillman, Theodore; and Gillman, Joseph: Powdered Stomach in the Treatment of Fatty Liver and Other Manifestations of Infantile Pellagra: Its Significance with Reference to the Problems of Edema and Steatorrhea in Infants and in Adults. Arch. Int. Med., **76**:63 (Aug.) 1945.

constant single pathologic lesion of infantile pellagra, occurring even with very mild symptoms.

Treatment with liver was somewhat more successful than with vitamins. A few infants slowly recovered on it. The first sign of recovery was the gradual loss of edema fluid. The liver tissue itself of the young patients improved more slowly than the clinical symptoms, and even after three to four weeks, when the children were discharged as clinically normal, considerable residual liver damage showed. Raw pancreas was also tried as treatment for the condition, and was followed by a similar slow improvement.

Remarkably rapid recovery of all of a group of cases followed the administration of small amounts of dried powdered hog stomach. Within two or three days after its use, there was a sudden loss of edema fluid followed by rapid healing of the skin lesions. Clinical cures were obtained in ten to fourteen days. Even the fatty livers were restored to normal after this treatment. The rapid improvement in all symptoms suggested to the authors that powdered stomach may be of considerable value in allied diseases of infants, such as celiac disease and other steatorrheas, or nutritional edemas. They note that among adults, sprue and idiopathic steatorrhea are also characterized by bulky, fatty stools, edema, and fatty liver.

Infantile pellagra once established, they say, induces secondary pathologic changes which do not disappear after vitamin therapy. The liver of young animals is much more susceptible to damage than that of old; and the liver in infantile pellagra is often almost avascular, as compared with the enormously vascular normal organ, which is capable of containing a large volume of fluid. The liver they consider directly concerned in water metabolism. A diuresis precedes by several days other signs of recovery from hepatic disease.

The stomach is involved early also in pellagra, and the stomach is important in water metabolism and edema. Biopsy specimens of stomach tissue, of course, were not obtained from these infants, though these might have shown severe cellular damage. There is an intimate relationship between the stomach, liver and kidney, according to Gillman and Gillman, in the maintenance of normal water metabolism. Powdered stomach, as they investigated it, had a remarkable lipotropic effect on the liver, and they say restored the normal gastro-hepato-renal relationship.

The pellagra described by Gillman and Gillman is a much more complex deficiency than the syndrome usually now called pellagra in America. It is of much interest that a severe deficiency disease with pellagra-like symptoms and with highly pathologic liver tissue, underwent remarkable remissions after treatment with powdered stomach and that normal liver tissue apparently was restored. One cannot help wondering about the effect of this substance in other edematous states or in other liver diseases. The reported recoveries following the use of powdered stomach are of much physiologic significance.

TWENTY-FIVE YEARS AGO

From Journals of 1920

Teaching of Medical Students.[1]—In the May number of the Southern Medical Journal * * * contributors lay great stress upon the need in medical schools as teachers of men in the active practice of medicine, and they point out the narrowing effect of the exclusive attention to hospital work and research which the full-time professor is supposed to give. Criticism highly derogatory to the clinical acumen of most of the recent graduates from the better medical schools is supported by allegations regarding the lack of the power to deal with patients these men showed when drafted into the Army * * *

The remedy advocated by most of the speakers for these conditions is the employment of active practitioners or consultants as teachers.

Permit me to point out that it was the failure of these very consultants and practitioners to teach adequately clinical medicine in the past which was the chief cause of the introduction of the full-time professor * * * to employ again as teachers active practitioners savors rather of a step backward than of an improvement * * *

The medical student has so vast a ground to cover that there is a great temptation for the teacher to concentrate his efforts rather upon covering the subject than upon seeing that the students do so * * *

The effort that should be made is toward the

1. Williams, Tom A.: Teaching of Medical Students. Correspondence. Sou. Med. J., **13**:780, 1920.

physiological interpretation of the signs and the combinations of signs.

Cesarean Section.[2]—The write has been impressed with the reckless resort to cesarean section prevalent in many quarters * * * In connection with this observation of a threatened cesarean "pandemic," we have been impressed with the average lack of professional ability noticeable among those practitioners whose obstetrical practices, though by no means large, embrace considerable numbers of cases terminating in delivery by the cesarean route * * *

A "gun toter" keeps on till he finds a human target. A man-eating tiger is never again satisfied with other food. And the physician who has once successfully * * * performed a cesarean section often behaves as though

"He on honey-dew hath fed,
And drunk the milk of Paradise" * * *

Among true obstetricians one's ability in that field is reckoned in inverse ratio to the number of cesarean sections which one is forced to do * * *

2. The Abuse of Cesarean Section. Editorial. Sou. Med. J., 13:828, 1920.

Book Reviews

Endocrinology of Woman. By E. C. Hamblen, B.S., M.D., F.A.C.S., Clinical Professor of Endocrinology and Associate Professor of Obstetrics and Gynecology, Duke University School of Medicine, Durham, North Carolina. 571 pages, illustrated. Springfield, Illinois: Charles C. Thomas, Publisher, 1945. Cloth, $8.00.

Instead of revising the progenitor of this book, "Endocrine Gynecology," which was published five years ago, knowledge of the subject had developed so rapidly that the author found it necessary to write a new book which he has called "Endocrinology of Woman." Naturally this contains many new findings in endocrinology and a somewhat more extended use of endocrine products.

The work would be justified if it contained only Dr. Hamblen's very original treatment of the poorly developed progestational phase of the endometrium in certain sterility cases by the use of the so-called "one-two gonadotropin" sequence, and the very clear outline of treatment for adolescent bleeding.

All the good material of the first book of course is retained in the very much improved successor, which has already become a reference book in wide use.

Gynecological and Obstetrical Urology. By Houston S. Everett, A.B., A.M., M.D., Associate Professor of Gynecology, the Johns Hopkins University, and Associate in Gynecology, the University of Maryland; Assistant Visiting Gynecologist and Gynecologist in Charge of the Cystoscopic Clinic, the Johns Hopkins Hospital. 517 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1944. Cloth, $6.00.

While many papers have been written upon this subject, and a few books, including a most comprehensive two-volume work by Kelly and Burnham called "Diseases of the Kidneys, Ureters, and Bladder," Dr. Everett has produced the most complete single volume extant on urology as applied to women. Notable among the chapters is one giving a detailed account of the simplest method of cystoscopy, with the Kelly instrument.

Trained under Dr. Guy L. Hunner, and for many years head of the Urologic Department of the Woman's Clinic of the Johns Hopkins Hospital, Dr. Everett has not only been able to condense the best in the literature but has given many original and practical ideas culled from his own practice. His discussion of ptosis of the kidney should be widely read in an age when suspension is often performed with more skill than study.

Little is found to criticize. As a first edition it suffers an occasional slip of the proof reader; and the index might be improved. For example, dysmenorrhea and dyspareunia, often encountered in ureteral stricture, are not listed in the index, although they are both admirably described in the text.

Tropical Medicine. By Sir Leonard Rogers, K.C.S.I., C.I.E., LL.D., M.D., B.S., F.R.C.P., F.R.C.S., F.R.S., Major-General, Indian Medical Service, Ret.; and Sir John W. D. Megaw, M.C.I.E., B.A., M.B., Hon. D. Sc. (Queen's University, Belfast), Major-General, Indian Medical Service, Ret. Fifth Edition. 518 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1944.

Rogers and Megaw's Tropical Medicine fulfills well in its fifth edition the expressed objective of the authors when in 1930 they first presented "a small work on tropical medicine which will contain only such details of microscopical technic as the general practitioner can carry out in his hospital or study, and will be devoted chiefly to the recognition and management of the diseases which are commonly met within tropical and subtropical countries." There is excellent discussion of the differential diagnostic features of related diseases which are grouped in separate sections devoted to diseases of protozoal, spirochetal, viral, rickettsial and bacterial origin, respectively, and to bowel diseases with diarrhea, diseases with prominent skin lesions, helminthic diseases, snake poisons, dietary and nutritional diseases, and diseases caused by heat and light.

As is generally true of British texts, this volume is clearly and readably written and fully covers each disease discussed with avoidance of excessive detail and dogmatism. Some American readers may object to the detailed presentation of the distribution of certain of the diseases of India and China, while a greater number will take exception to the concept that vitamins act as neutralizing agents of toxins originating from food stuffs,

especially in view of mounting evidence of their essential role in cellular biochemical processes. These defects are minor, however, in a comprehensive, lucid volume.

A Manual of Surgical Anatomy. Prepared under the auspices of the Committee on Surgery of the Division of Medical Sciences of the National Research Council by Tom Jones and W. C. Shepard. Cloth. Price $5.00. 195 pages. 267 illustrations on 138 figures; 153 in colors. Philadelphia and London: W. B. Saunders Company, 1945.

This atlas of surgical anatomy is one of a series developed under the auspices of the Division of Medical Sciences of the National Research Council, as a reference work for the military surgeon. The illustrations were drawn by Tom Jones and W. C. Shepard who had prepared a similar manual during the first World War. The manual consists entirely of illustrations, there is no concomitant text. There is a very complete explanatory index of more than 50 pages, however, which gives a short description of the anatomical structures that appear in the atlas, including origin and distribution of arteries and nerves.

The drawings are excellent and very clear. Many of them surpass the limit of an atlas of anatomy and approach that of an atlas of surgical operations. There are many cross sections which are quite helpful in the understanding of complicated anatomical relations.

The authors seem to be especially interested in the technic of thoracic and abdominal sympathectomy which are represented by a goodly number of illustrations in the atlas, as is the technic of thoracotomy, perhaps at the expense of some more common typical operations. The manual was prepared for the use of army surgeons which, of course, limits its usefulness to the surgeon in civilian practice. To mention just one important omission: the female pelvis has not been illustrated in the atlas at all.

As a whole, the manual will certainly serve its purpose which is, as stated in a preface by the Surgeon General, to ". . . become a valuable, if not indispensable, reference for the military surgeon . . . as well as the civilian surgeon concerned with the surgery of trauma."

Proceedings of the Rudolf Virchow Medical Society in the City of New York. Volume III, 1944. Edited by the Publication Committee. 103 pages. New York: Brooklyn Medical Press, Incorporated. Cloth $2.00.

This is a publication of the Rudolph Virchow Medical Society of New York which originally was a society of physicians of German origin. It has now in its ranks a number of émigre physicians from European countries, some of them quite prominent in their respective fields.

The "Proceedings" are a collection of papers read at the meetings of the society. Most of them are too sketchy to justify a detailed discussion. There is a good article on "Coronary Insufficiency," another one on traumatic injuries of the heart and lungs. Several obituaries are quite noteworthy, especially the one on Eugen Steinach of rejuvenation fame.

It is interesting to watch the work done by the members of a group of identical origin. Some of these men represent valuable additions to American medicine.

A National Health Service. Presented by the Minister of Health and the Secretary of State for Scotland to Parliament by Command of His Majesty. February 1944. 85 pages. American Edition reproduced photographically from the English edition and published by arrangement with His Majesty's stationery office. New York: The Macmillan Company, 1944.

Because of the current interest in schemes for national health, this survey by the Department of Health for Scotland is a timely informative and authoritative review of the British plans including all phases of the problem. Reading of it arouses speculation on how such a scheme might affect medicine in the United States. State medicine in the United States during the past 30 years has consisted of the charity hospitals and of the endowed and teaching institutions, and of the public health and industrial medical services. This has been feudal in that it has deprived the poor patient of a free choice of physician, and given those with low incomes no alternative but to accept. Much of the charity work in the United States is done by the intern or resident with no choice whatsoever on the part of the patient. Furthermore, every physician in practice does a large amount of charity work in his own office.

The National Health Service scheme is based upon the principle that the charity or part-pay patient will be covered by insurance so that he may select his physician and his hospital. The adoption of such a scheme in the United States would so greatly increase the medical services that perhaps an additional 50,000 physicians besides those in the armed services would be needed to carry out the plan properly. It would also permit private hospitals to take part-pay or insured patients on a ward basis to an extent never realized before. This would improve the teaching services for interns and visiting physicians.

The increased volume of work with which every popular physician would be burdened would probably force the clinic practice of medicine on the majority of our practitioners. Some men might be forced to increase their fees until they would usually not be available for the insured patient. It is believed that the physician-patient relationship would be encouraged rather than hindered and that the income of physicians generally would be increased. This should be true of the hospitals as well. A great body of our citizens who receive little or no medical care at the present would feel entitled to various specialty and hospital services. If the insurance scheme provides for research and preventive medicine as that for Scotland does, a great increase in the amount and quality of research in the hospital and public health fields might be forthcoming. The charity hospital as such would disappear. An important problem would be the ethics of how a busy physician, who formerly did

little or no part-pay work, would meet the greatly increased volume of part-pay patients who might apply to him for treatment. This review for a national health service is thought-provoking and is good reading for an unbiased appraisal of the situation in the British Isles. It offers no panacea for bureaucracy which is the principal weakness of the scheme.

Anatomy As a Basis for Medical and Dental Practice. By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C., Professor of Anatomy, Dalhouse University, Halifax, N. S., Canada. 863 pages. New York: Paul B. Hoeber, Incorporated. Cloth, $7.50.

The approach to the teaching of anatomy as advocated by Dr. Mainland is not only revolutionary but is greatly to be praised. The author is a physician and knows something of clinical medicine, which he interjects into almost every sentence on the description of anatomic parts. In fact, the whole book is a refreshing anatomic-clinical conference. He introduces radiography and fluoroscopy as among the most important tools for the study of anatomy. He further discloses a knowledge of biometry and shows that all phases of anatomy are subject to wide ranges of normal variation, facts known to the pathologists and radiologists for more than 25 years, but which have been unknown or only dim concepts in textbooks of anatomy. He also integrates these constitutional variations with the incidence of disease, a subject which would warm the heart of Dr. Wade Hampton Brown were he still alive. The very acceptance of the fact that no human being has the modal values for all anatomic structures and that human individuality is made up of combinations of certain hereditary and acquired variations from the mode makes anatomy a living subject.

It is the opinion of the reviewer, who taught anatomy for some years, that the decadent state of gross anatomy in the United States during the past 25 years has been due to the staffing of departments of anatomy in medical schools with doctors of philosophy who have no concept of clinical medicine, or with physicians who spend the 40 to 50 years of their anatomic life forgetting all of the clinical medicine and pathology that continuous isolation in the dissecting room can produce. The main trouble with the use of Dr. Mainland's book in American medical schools will be that many staffs of anatomy are not mentally equipped to teach the subject as he has outlined. To teach anatomy as a living subject, as Dr. Mainland suggests, will require that the teaching staffs of gross anatomy do autopsies, x-ray examinations, and anatomic-clinical conferences as a regular part of their duties, stressing the importance of anatomic or physiologic variation on the incidence and type of disease. It will also be necessary for the histologist to be familiar with histo-pathology and to be as conscious of histologic variations on the incidence of disease and the maintenance of health as is the histopathologist. Congratulations are due Dr. Mainland for his revolutionary and sensible approach to the teaching of anatomy. May his kind increase.

Southern Medical News

THE OKLAHOMA CITY CLINICAL SOCIETY

The Oklahoma City Clinical Society will hold its fifteenth annual conference in Oklahoma City, November 26-29. The Society has secured for this conference sixteen guest speakers who are physicians well qualified to present their respective subjects. (See page 62 for formal announcement and names of speakers.) The registration fee of $10.00 includes all the general assemblies, round table luncheons, dinner meetings, postgraduate courses, and the annual smoker. Officers of the Clinical Society are: Dr. C. P. Bondurant, President; Dr. Clark H. Hall, Director of Clinics; Dr. L. Chester McHenry, Vice-President; Dr. Elmer R. Musick, Secretary; and Dr. Ben H. Nicholson, Treasurer. Executive Committee: Dr. Wendell Long, Dr. Basil A. Hayes, Dr. W. F. Keller, Dr. J. H. Robinson, Dr. D. H. O'Donoghue and Dr. Gregory E. Stanbro. For additional information write the Secretary, 512 Medical Arts Building, Oklahoma City 2, Oklahoma.

ALABAMA

Dr. Luther L. Hill, Montgomery, Lieutenant Colonel, Medical Corps, recently assumed the position of Base Surgeon, Sedalia Army Air Field, a First Troop Carrier Command installation near Warrensburg, Missouri. Prior to this position he served in a like capacity at Bergstrom Field, Texas.

Dr. Paul S. Woodall, Birmingham, Lieutenant Colonel, Medical Corps, for the past three years Post Surgeon and Commanding Officer of station hospitals at Myrtle Beach, South Carolina, Army Airfield and Will Rogers Field, Oklahoma, is being separated from service, and recently was appointed Assistant Professor of Obstetrics and Gynecology, The Medical College of Alabama, Birmingham. Before resuming his private practice and duties on the Medical School faculty the first of the year, Dr. Woodall plans to do special work at several clinics.

DEATHS

Dr. Samuel Watt Riggs, Pleasant Hill, aged 74, died recently of coronary thrombosis.

Dr. Mack Milton Strickland, Selma, aged 69, died recently of cardiac failure due to hypertensive heart disease.

ARKANSAS

Tenth Councilor District Medical Society has elected Dr. Geo. M. Love, Rogers, President; Dr. W. G. Eberle, Fort Smith, Vice-President; and Dr. Ralph E. Crigler, Fort Smith, Secretary-Treasurer.

Southeast Arkansas Medical Society has elected Dr. S. C. Clark, Lake Village, President; and Dr. M. C. Crandall, Wilmot, Secretary.

Dr. W. P. Scarlett, Little Rock, has assumed duties as City Health Officer.

Dr. I. H. Jewell, Paris, has been elected Surgeon of the local American Legion Post.

Dr. H. K. Wright, who has been in military service, has opened offices in the Medical Arts Building, Hot Springs National Park, for practice of general surgery.

Dr. J. J. Delaney, Fayetteville, has been elected Surgeon of the local American Legion Post.

Dr. J. L. Bean, Lincoln, has moved to Stilwell.

Dr. W. H. Abington, Beebe, has been elected Surgeon of the local American Legion Post.

Dr. Julius H. Hellums, Dumas, who has been in military service for more than four years, has been released and has returned to practice at Dumas.

Dr. S. T. Trice, Dierks, has moved to Center Point.

Dr. Friedman Sisco, Springdale, after over four years in military service as Major, Medical Corps, Army of the United States, has been released and has returned to practice at Springdale.

Dr. Marion Bates Leverett, McGehee, and Miss Betty Jane Perryman, Fort Smith, were married recently.

Dr. Henry Thomas Gray, Forrest City, and Miss Johanna Janke, Ponca City, Oklahoma, were married recently.

Dr. James Bates Kittrell and Miss Ruth Estelle Hendrick, both of Texarkana, were married recently.

DEATHS

Dr. Wallace Linn Brittain, Conway, aged 41, died September 4.

Continued on page 62

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Continued from page 772

Dr. Clyde Baker Callen, Fayetteville, aged 61, died recently of metastatic cancer and arthritis.

DISTRICT OF COLUMBIA

Dr. William Arthur Morgan, Washington, will have named in his honor a 180-bed hospital under construction in Ciudad Trujillo, Dominican Republic, this in recognition of the humanitarian services rendered by Dr. Morgan on a visit to that country early this year. Certain rooms in the hospital will be reserved for Dr. Morgan, who will return to the West Indies for several months annually and will be present for the dedication ceremony at the end of this year.

St. Elizabeth Hospital, Washington, has promoted Dr. Samuel A. Silk to First Assistant Physician and Dr. Addison M. Duval to Clinical Director.

Dr. George C. Dunham, Major General, Washington, President of the Institute of Inter-American Affairs, has been awarded the distinguished service medal for his work in advancing the development of Latin America. He has been with the Office of Inter-American Affairs since 1942.

Dr. Benjamin I. Weininger will replace Dr. Michael J. Miller as head of the new District of Columbia Alcoholic Clinic, Washington.

Deaths

Dr. Jesse Shoup, Washington, aged 80, died recently.

FLORIDA

Florida Radiological Society at its recent meeting held at Orlando elected Dr. John A. Pines, Orlando, President; Dr. Charles M. Gray, Orlando, Vice-President; and Dr. James F. Pitman, Lake City, Secretary-Treasurer.

Dr. Wilson T. Sowder, U. S. Public Health Service, a graduate of the University of Virginia Department of Medicine, Charlottesville, in 1932, has been appointed Health Officer of Florida, succeeding Dr. Henry Hanson, Jacksonville, who retired recently.

GEORGIA

Emory University School of Medicine, Atlanta, announces the following changes in the medical faculty: Dr. William Frank Friedewald, associated since 1943 with the International Health Division, Rockefeller Foundation, was named Professor of Bacteriology and Chairman of the Department, succeeding Dr. Roy R. Kracke, now Dean, The Alabama College of Medicine, Birmingham, Alabama; Dr. William C. Warren, formerly Associate Professor of Clinical Otolaryngology, was appointed Professor of Otology and Rhinolaryngology and Chairman of the Department, succeeding Dr. Calhoun McDougall; Dr. R. Morris Paty was appointed Professor of Surgery and Acting Head of the Department of Surgery, continuing as Associate Dean of the School of Medicine; Dr. Harry R. Lipton, Assistant in Psychiatry, was appointed Instructor in Psychiatry, and Dr. Marion Hester, formerly a resident at Grady Hospital, Atlanta, as Instructor in Opthalmology.

Dr. J. C. Patterson, Cuthbert, has been appointed to the State Board of Health.

Dr. George H. Noble, Atlanta, will locate at Monroe for practice of medicine.

Dr. Thomas M. Hall, Milledgeville, a few months ago celebrated his seventy-fourth birthday.

Continued on page 64

ANNOUNCING THE FIFTEENTH ANNUAL CONFERENCE OF THE OKLAHOMA CITY CLINICAL SOCIETY

November 26, 27, 28, 29, 1945

DISTINGUISHED GUEST LECTURERS

LEWIS G. ALLEN, M.D., RADIOLOGY, Professor of Clinical Radiology, University of Kansas School of Medicine, Kansas City, Kansas.

WALTER PUTNAM BLOUNT, M.D., ORTHOPEDIC SURGERY, Governing Staff, Columbia Hospital; Milwaukee Children's Hospital; Milwaukee County Hospital and Johnston Emergency Hospital, Milwaukee, Wisconsin.

LOUIS A. BRUNSTING, M.D., DERMATOLOGY, Associate Professor of Dermatology and Syphilology, University of Minnesota Graduate School, Mayo Clinic, Rochester, Minnesota.

RICHARD B. CATTELL, M.D., SURGERY, Surgeon, Lahey Clinic, Boston, Massachusetts.

WARREN HENRY COLE, M.D., SURGERY, Associate Dean, University of Illinois, College of Medicine; Professor and Head of the Department of Surgery, Chicago, Illinois.

VIRGIL S. COUNSELLER, M.D., SURGERY, Professor of Surgery, Mayo Foundation, University of Minnesota School of Medicine, Rochester, Minnesota.

CHARLES BRENTON HUGGINS, M.D., UROLOGY, Professor of Surgery, University of Chicago, School of Medicine, Chicago, Illinois.

ERNEST E. IRONS, M.D., INTERNAL MEDICINE, Professor of Medicine, University of Illinois School of Medicine, President, American College of Physicians, Chicago, Illinois.

RAYMOND WILLIAM McNEALY, M.D., SURGERY, Associate Professor of Surgery, Northwestern University Medical School, Chicago, Illinois.

AVERY D. PRANGEN, M.D., OPHTHALMOLOGY, Associate Professor of Ophthalmology, Mayo Foundation, University of Minnesota School of Medicine, Rochester, Minnesota.

JEAN PAUL PRATT, M.D., GYNECOLOGY, Surgeon-in-Charge, Division of Gynecology and Obstetrics, Henry Ford Hospital, Detroit, Michigan.

CHESTER A. STEWART, M.D., PEDIATRICS, Director of Pediatrics, Louisiana State University School of Medicine, New Orleans, Louisiana.

CHARLES TURNER STONE, M.D., INTERNAL MEDICINE, Professor of Medicine, Chairman Department, Internal Medicine, University of Texas School of Medicine, Physician in Chief, John Sealy Hospital, Galveston, Texas.

THEODORE E. WALSH, M.D., OTOLARYNGOLOGY, Professor of Otorhinolaryngology, Washington University School of Medicine, St. Louis, Missouri.

FRANK E. WHITACRE, M.D., OBSTETRICS, Professor and Head of Department of Obstetrics and Gynecology, University of Tennessee School of Medicine, Memphis, Tennessee.

S. MARX WHITE, M.D., INTERNAL MEDICINE, Emeritus Professor of Medicine, University of Minnesota School of Medicine, Minneapolis, Minnesota.

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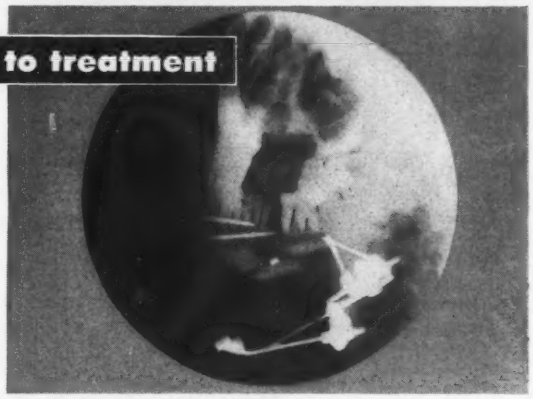

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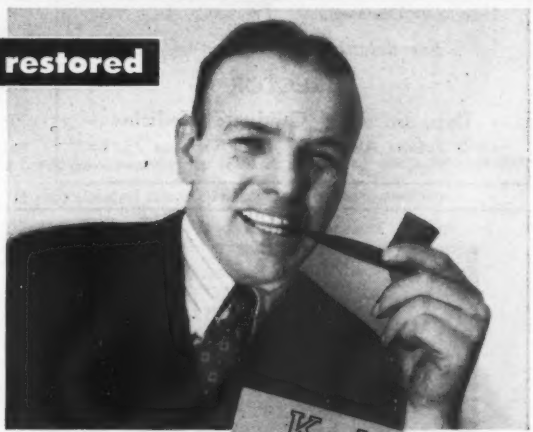

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RADIOGRAPHY

"blueprint" to surgical procedure

Continued from page 62

Dr. John T. Akin, Jr., Atlanta, announces the opening of his offices for the practice of surgery in the Medical Arts Building, associated with Dr. Floyd W. McRae.

Dr. W. P. Smith, Bowdon, who has practiced medicine fifty-four years, recently celebrated his seventy-ninth birthday.

Dr. J. Frank Harris, Atlanta, announces the opening of his office for the practice of internal medicine in the Medical Arts Building.

Dr. Eugene Rollin Corson, Savannah, recently celebrated his ninetieth birthday.

Dr. Clifton G. Kemper, Atlanta, announces the new location of his offices in the Doctors Building.

Dr. Philip A. Mulherin, Augusta, recently discharged from the Army, is Chairman of the Department of Pediatrics, University of Georgia School of Medicine, succeeding the late Dr. Claude M. Burpee.

The Tulane University of Louisiana

School of Medicine

POSTGRADUATE COURSES

Traumatic and Emergency Surgery ..... November 5-10, 1945
Pediatrics ..... December 10-14, 1945
Tropical Medicine and Parasitology ..... December 10-21, 1945
Tropical Medicine and Parasitology ..... January 2 to May 25, 1946
Obstetrics and Gynecology ..... January 14-18, 1946
Infectious Diseases ..... February 11-15, 1946

For detailed information write

DIRECTOR

Department of Graduate Medicine

1430 Tulane Ave. New Orleans 13, La.

Dr. Herbert M. Olnick, Dahlonega, Physician to the North Georgia College, has bought the Clinic Building which will be a permanent and convenient medical center for the college students and the public.

Dr. DeWitt T. Bond, Danielsville, recently discharged from the Army, has opened an office in Danielsville for the practice of medicine.

Milledgeville State Hospital, Milledgeville, has increased its staff members to twenty-one with the appointment of five new ones as follows: Dr. J. D. Combs, Muncie, Indiana; Dr. L. E. Pennington, Madison, Wisconsin; Dr. Robert B. Quattlebaum, Savannah; Dr. Jack B. Moon, Augusta; and Dr. Veronica Murphy, Indianapolis, Indiana.

Dr. Milton Thomas Edgerton, Jr., Atlanta, and Miss Patricia Jane Jones, Forrest Hills, Long Island, New York, were married recently.

DEATHS

Dr. Harry Ainsworth, Thomasville, aged 68, died recently.
Dr. Bolling Sasnett Branham, Powder Springs, aged 64, died recently.
Dr. J. H. Campbell, Commerce, aged 55, died recently.
Dr. Joel Toy Curry, Macon, aged 74, died recently.
Dr. Jackson Cleveland Loveless, Grayson, aged 55, died recently.
Dr. Lyman Sanderson Osborne, Fitzgerald, aged 90, died recently.
Dr. Eugene Farmer Sanford, Buchanan, aged 55, died recently.
Dr. Benjamin L. Smith, Forsyth, aged 62, died recently.
Dr. Roger C. Swint, Atlanta, aged 70, died recently.

KENTUCKY

Kentucky State Medical Association held its annual meeting at Lexington, October 29-31.

Dr. Guy Zimmerman, Jr., Mount Sterling, and Miss Margaret Wells, Nashville, Tennessee, were married recently.

Dr. Edwin Clarence Morgan and Miss Marjorie Larman, both of Russellville, were married recently.

DEATHS

Dr. Edith May Cole, Louisville, aged 61, died recently of carcinoma of the uterus.
Dr. Thomas Leonard Lamkin, Clinton, aged 72, died recently.
Dr. Corlis H. Wallin, Brooksville, aged 72, died recently.

LOUISIANA

Dr. Urban Maes, Director and Professor of Surgery, Louisiana State University School of Medicine, New Orleans, who organized the 64th General Hospital, has received word that the Meritorious Service Unit Plaque was presented to this unit at ceremonies July 25, 1945 at Livorno, Italy.

Dr. Wilbur C. Smith, who has taught anatomy for twenty-seven years at Tulane University School of Medicine, New Orleans, has been made Dean of the Louisiana State University School of Medicine, succeeding Dr. Beryl I. Burns, resigned effective September 1.

Dr. William B. Wendell, Associate Professor of Chemistry, University of Tennessee, has been appointed Professor and Head

Continued on page 66

LaMOTTE COMBINATION BLOOD CHEMISTRY OUTFITS

To meet the request of many physicians, the LaMotte Research Department has developed these compact outfits. They are ideal where space is limited. The outfit illustrated contains all necessary apparatus, reagents, etc., for determining gastric acidity, blood sugar, blood urea, icterus index, and phenolsulfonphthalein renal efficiency. Price of outfit illustrated above, $67.50 f.o.b. Towson. Similar units containing other combinations of standard LaMotte tests can be furnished. Full information will be sent on request.

LaMOTTE CHEMICAL PRODUCTS CO.

Dept. S Towson 4, Baltimore, Md.

THE new light became visible like a dazzling meteor in the evening of the nineteenth century. It surrounded the morning of our own century with the rosy light of hope and promise. Like a glittering sun it shines resplendent on the working day of the twentieth century, revealing new fairways and fresh horizons in nearly every land in the world of science. . . . **In commemorating William Conrad Roentgen this year—the centennial of his birth, also the semi-centennial of his discovery of the x-ray—one is inspired anew by the above tribute spoken by Dr. Gosta Forssell, of Stockholm, Sweden, before the Fifth International Congress of Radiology, held in Chicago in 1937.**

OUR FIFTIETH YEAR OF SERVICE

GENERAL ELECTRIC X-RAY CORPORATION

Continued from page 64

of the Department of Biochemistry, Tulane University School of Medicine, succeeding Dr. Sydney Bliss.

Dr. Benjamin T. Galloway is the recipient of the Walter Reed Memorial Medal, given by the Louisiana State Medical Society to the graduate presenting the best thesis either on tropical or preventive medicine.

Dr. Roy H. Turner, New Orleans, Colonel, Medical Corps, U. S. Army, formerly Communicable Disease Treatment Branch, Medical Consultants Division, has been assigned overseas.

Dr. Jesse F. Tanner, Bernice, has been appointed coroner of Union Parish, completing the unexpired term of the late Dr. J. G. Taylor, Farmerville.

Alton Ochsner Medical Foundation for research, New Orleans, has received a grant of $5,000 from Smith, Kline and French Laboratories, Philadelphia, Pennsylvania, to continue the work on enzymes, which is being done by Dr. Otto Schales, Director of the Chemical Research Laboratory.

Dr. George Peyton Kelley and Miss Bessie Browder, both of Shreveport, were married recently.

Deaths

Dr. Edward Francis Bacon, New Orleans, aged 70, died recently.

Dr. Edward Andrew Grice, Epps, aged 71, died recently.

Dr. Domenico Merendino, New Orleans, aged 72, died recently of cerebral hemorrhage and arteriosclerotic heart disease.

Dr. Merrick Ward Swords, New Orleans, aged 61, died recently of coronary thrombosis.

Dr. J. G. Taylor, Farmerville, aged 77, died recently.

Dr. Waddy Thompson Wilkinson Jr., Coushatta, aged 42, died recently.

Dr. Frank Fenwick Young, Covington, aged 82, died September 26 of cardio-vascular-renal disease.

MARYLAND

The Baltimore Rh Typing Laboratory has been established by the Obstetrical and Gynecological Section of the Baltimore City Medical Society, located in the Bressler Research Building. The President of the Section, Dr. M. Alexander Novey, appointed a committee of three to act as a Board of Directors for the Laboratory and to be responsible to the Society: Dr. Alan F. Guttmacher, Dr. Hugh B. McNally and Dr. I. A. Siegel.

Dr. Charles N. Davidson, Baltimore, has been appointed temporary head, Department of Radiology, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, pending the return of Dr. Walter L. Kilby from military service. Dr. Henry J. Walton, who had been Professor since 1918 until a few years ago when he was made Professor Emeritus, has been serving since Dr. Kilby entered the service.

MISSISSIPPI

At the recent third quarterly meeting of the Northeast Mississippi Thirteen Counties Medical Society at Amory, Dr. G. S. Bryan, Amory, Dr. W. A. Evans, Aberdeen, Dr. J. Rice Williams, Houston, and Dr. W. C. Walker, Houlka, were made honorary members.

Dr. Emma Gay, Biloxi, former State Commander of the American Cancer Society, has accepted the responsibility for the regional medical education program of the American Cancer Society at the state office in the Lorenza Building, Jackson. She will serve as District Commander and member of the State Executive Committee, of which Dr. Felix J. Underwood is Chairman.

Dr. Samuel Clark Atkinson, Drew, and Miss Marjorie Sturtevent Webb were married recently.

Deaths

Dr. M. E. Arrington, Vaiden, aged 39, died recently from injuries received in an automobile wreck.

MISSOURI

Missouri State Medical Association will hold its 1946 annual session March 24-26, at the Jefferson Hotel, St. Louis.

Board of Health of Cape Girardeau County has appointed Dr. R. A. Rittner and Dr. O. L. Seabaugh, Cape Girardeau, members.

Dr. Conrad S. Sommer, Superintendent of the state division of mental hospitals in Illinois from 1940-1943 and recently Director of Mental Hygiene Service of the Illinois Department of Public Welfare, has resigned the latter position to accept an

Continued on page 68

The New Emmert-Gellhorn Pessary

An improved device for treatment of inoperable uterine prolapse

For use in cases of inoperable uterine prolapse, this new pessary is offered as an improvement upon the well-known Gellhorn Pessary, long used with great success. The Emmert-Gellhorn Pessary is made of one solid piece of Neicomold, a synthetic material that may be boiled. The material is unbreakable and stays smooth in use since it is unaffected by the genital secretions. Neither does it affect or irritate the vaginal mucosa. The shape is approximately that of a mushroom, with the upper surface slightly depressed.

Instead of a solid stem, the Emmert-Gellhorn Pessary employs a stem having a hole drilled throughout its length. This offers the considerable advantage of drainage, preventing accumulation of dammed-up secretions. This permits fewer removals of the pessary for cleaning, of great benefit to the patient, particularly since many of those using this pessary are aged and find such frequent manipulation and visits to the physician a severe handicap.

The stem of the new pessary is ¼ inch shorter than that of the former pattern, and does not terminate in the knob formerly used. A slight hollowing of the stem near the end, however, allows easy grasp for removal. In weight, the Emmert-Gellhorn Pessary has the advantage of being considerably lighter. This decreased weight also adds to the comfort of the patient.

PRICE—JE5162 — Emmert-Gellhorn Pessary, Diameter 2 or 2½ inches, STATE SIZE, Each $2.25

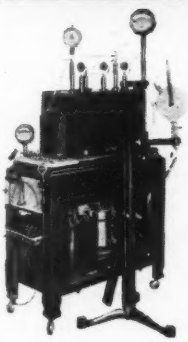
SPECIAL SIZES: 2¼, 2¾ or 3-inch may be had on order, at each $2.75

A. S. ALOE COMPANY

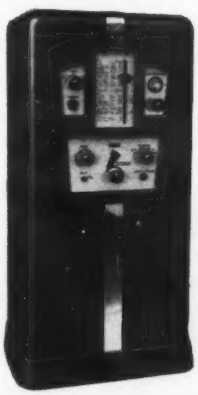
1831 OLIVE STREET, ST. LOUIS, MO.

A *Salute* TO ROENTGEN

...and a PLEDGE for the FUTURE



As early as 1905 Keleket perfected this "Grosse Flamme" X-ray coil, so called because it "drew a flame of 12 inches" when other coils produced but a few inches of spark.



The KELEKET Techron with its many patented features, is acknowledged to be the greatest advancement in X-ray control units. In the entire field of X-ray there is nothing that compares with the Techron Control!

IT is now 50 years since Wilhelm Konrad Roentgen discovered the X-ray. From this discovery came a great new instrument of medicine—the means of saving thousands of human lives.

But the X-ray of today is very different from the X-ray of Roentgen's period. For 50 years, it has been improved—refined—perfected. To all those who have carried on the work of Roentgen, credit is also due.

KELEKET, oldest company continuously in X-ray, was in business within five years of Roentgen's discovery. KELEKET and X-ray grew up together. And KELEKET pioneered the way through the crude apparatus of the early 1900's, just as it leads the way in the splendid equipment of today.

In saluting the achievement of Roentgen, KELEKET also offers a pledge for the future. KELEKET'S work has more than merely a commercial significance. For the products of the KELEKET Company are closely associated with the advancement of medical science and the preservation of human life.

THE KELLEY-KOETT MANUFACTURING CO., W. FOURTH ST., COVINGTON, KY.

KELEKET X-RAY

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Foe of Infection

Iodine Educational Bureau, Inc.
120 Broadway, New York 5, N. Y.

★ ★

Continued from page 66

appointment as Assistant Clinical Professor of Psychiatry, Washington University School of Medicine, St. Louis, and to develop a psychiatric clinic at the St. Louis County Hospital, Clayton.

Dr. John W. Stewart, St. Louis, Colonel, Medical Corps, U. S. Army, has been awarded the Legion of Merit.

Dr. Kenneth V. Larsen, St. Louis, Lieutenant Colonel, Medical Corps, U. S. Army, has been awarded the Bronze Star.

Dr. Edward N. Zinschlag, St. Louis, Captain, Medical Corps, U. S. Army, has been decorated with the Silver Star.

Dr. Richard Frederick Auler, St. Louis, and Miss Lillian Pauline Haugen, Madison, Wisconsin, were married recently.

Dr. Frank J. Kelly, Kansas City, and Miss Dorothy Rita Paige, St. Louis, were married recently.

Dr. Clarence Ray Leininger Jr., Trenton, and Miss LoDonna Watson, Rexburg, Idaho, were married recently.

Dr. John William Murphy Jr., Kirkwood, and Miss Elizabeth Anne White, Norfolk, Virginia, were married recently.

Deaths

Dr. John L. Benage, Lebanon, aged 70, died recently of cerebral hemorrhage.

Dr. Joseph Blickensderfer, Lebanon, aged 82, died recently of myocarditis.

Dr. Charles A. Talbot, Waynesville, aged 65, died recently of cerebral hemorrhage.

Dr. Alonzo Clinton Ward, Osceola, aged 89, died recently of cerebral hemorrhage.

Dr. Alexander W. Widner, Newtown, aged 76, died recently of pneumonia and coronary thrombosis.

Dr. Bohumil Joseph Wiesner, St. Louis, aged 72, died recently.

Dr. Robert Edward Wilson, St. Louis, aged 74, died recently of carcinoma of the bladder.

Dr. Robert R. Cutler, Washington, aged 57, died recently.

Dr. Posey D. Gum, West Plains, aged 73, died recently.

Dr. Walter Baumgarten, St. Louis, aged 72, died recently.

Dr. Harrison S. Hickok, Kansas City, aged 76, died recently.

Dr. Jules M. Brady, St. Louis, aged 69, died recently.

Dr. Carroll Smith, St. Louis, aged 67, died September 6.

NORTH CAROLINA

Bowman Gray School of Medicine, Winston-Salem, announces the following appointments: Dr. J. E. Hawkins, formerly Instructor in Physiology and special research associate in the psychoacoustic laboratory, Harvard Medical School, as Assistant Professor of Physiology and Pharmacology; Dr. R. P. Morehead, Associate Professor of Pathology, as Director of the Department of Pathology and Bacteriology to succeed Dr. C. C. Carpenter, who asked to be relieved of the direction of the Department. Dr. Carpenter continuing a member of the staff of the Department with title of Professor of Legal Medicine and Director of the Laboratory of Clinical Pathology.

Dr. W. H. Fishman, Assistant Professor of Biochemistry, Bowman Gray School of Medicine, Winston-Salem, has resigned to accept position of Research Associate in the Departments of Surgery and Biochemistry at the University of Chicago School of Medicine.

Dr. Charles M. Norfleet, Jr., who has received his discharge from the Army after serving three years in India, has resumed his position as Instructor in Urology, Bowman Gray School of Medicine, Winston-Salem.

Department of Internal Medicine, Bowman Gray School of Medicine, Winston-Salem, has received a grant of $7.000 awarded by the John and Mary R. Markle Foundation for research under the direction of Dr. George T. Harrell, Jr.; and the Department of Physiology has been awarded a grant of $400 by the Council on Pharmacy and Chemistry of the American Medical Association to support research of Dr. Harold D. Green on the influence of environmental temperature on ischemic compression shock.

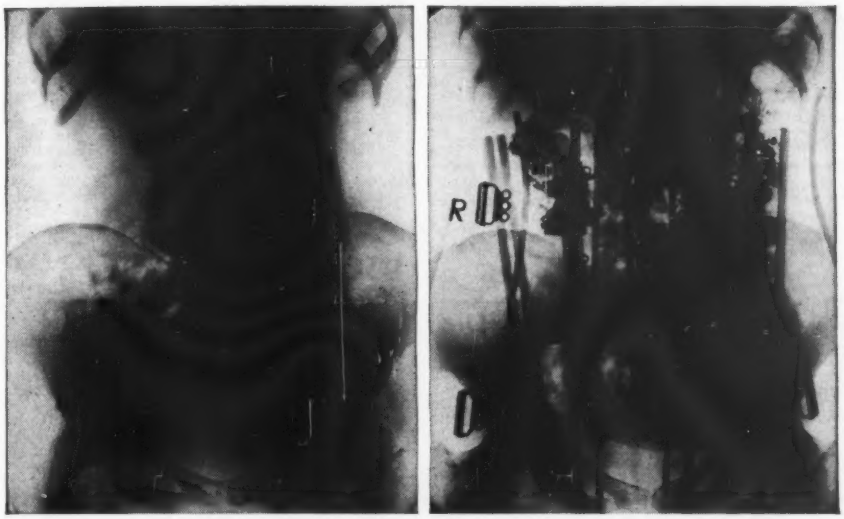
Moore General Hospital, Swannanoa, and the United States Army General Hospital, Camp Butner, near Durham, have been designated as centers for treatment and research on tropical skin diseases.

Mr. Eden Clark, Duke University, Durham, has been named Chairman of the Board of Governors of the Association of Medical Illustrators.

Dr. Alfred Mordecai has been appointed Health Officer for the newly created health department (Davie, Yadkin and Stokes Counties) with headquarters in Winston-Salem.

Continued on page 70

WHEN *digestive symptoms and general malaise are accompanied by marked downward displacement of the viscera, they are often relieved by* ANATOMICAL SUPPORT.



X-Ray of patient with visceroptosis. (Left) The lesser curvature of the stomach is below the crests of the ilia. (Right) X-Ray of same patient after application of Camp Support for visceroptosis indicating how the viscera is held in a more nearly normal position.

Visceroptosis Support – CAMP

The roentgenologist may or may not find disturbed conditions in the duodenum... the displaced viscera being the only finding. For these patients, many physicians prescribe adequate rest, proper food at regular intervals, graduated exercises (especially for the patient with "visceroptotic habitus"), and a scientifically designed anatomical support. Numerous reports show that this treatment results in the gradual disappearance of the digestive symptoms with improvement in general health and weight gains for the thin patient. In time the support may be discarded.

Camp supports for visceroptosis are fitted and adjusted with the patient in the partial Trendelenburg position. Pads are frequently used under the direction of the physician.

Camp Supports are also of assistance for postural defects that so frequently accompany the visceroptotic condition.

S. H. CAMP & COMPANY • Jackson, Mich. • *World's Largest Manufacturers of Scientific Supports*

Offices in NEW YORK • CHICAGO • WINDSOR, ONTARIO • LONDON, ENGLAND

Continued from page 68

Dr. W. C. Davison, Dean, Duke University School of Medicine, Durham, has been appointed Medical Advisor for the medical re-education program in the European occupied countries, with headquarters probably in Germany.

Caldwell Hospital, Lenoir, has elected Dr. Clyde R. Hedrick, Lenoir, President, succeeding the late Dr. J. E. Rudisill, co-founder of the hospital. Dr. Fred Hubbard, North Wilkesboro, Dr. L. N. Glenn, Gastonia, and Dr. Frank Jones, Newton, will take care of the surgery until arrangements can be made to secure a resident surgeon.

Dr. Gilcin F. Meadors, Jr., has resigned as Health Officer of Lenoir County to report to the States Relation Division of the U. S. Public Health Service, Washington, D. C.

Dr. Hamilton W. Stevens, Jacksonville, has resigned as Director of the Onslow-Pender District Health Department, to become Director of the Wilson City and County Health unit.

Dr. George M. Kozeruba, Wilmington, and Miss Berniece Carey, New Orleans, Louisiana, were married recently.

Dr. Matthew A. Stroup, Cherryville, and Dr. Frances P. Shaw, Oxford, Mississippi, were married recently.

SOUTH CAROLINA

Dr. J. Decherd Guess, Greenville, succeeds Dr. J. W. Jervey who resigned as Editor of *The Bulletin of the Greenville County Medical Society.*

Dr. R. M. Pollitzer, President of the staff of Greenville General Hospital, has appointed a Committee on Hospital Expansion to serve as consultants or advisors to the Board of Governors in the matter of hospital planning and building, the members of the committee being Dr. Frank Daniels, Dr. J. D. Guess, Dr. J. Warren White, Dr. George Wilkinson, and the President, Dr. Pollitzer, ex-officio.

Dr. W. West Simmons, Greenville, after four years with the United States Public Health Service, has opened offices and will limit his work to anesthesia.

Dr. Elbert J. Dickert, a native of Newberry, South Carolina, and a graduate of Tulane University School of Medicine, New Orleans, Louisiana, has joined the Resident Staff, Columbia Hospital, Columbia.

Dr. Paul A. Woods, formerly Assistant Director, Richland County Health Department, has been appointed Acting Health Officer of Aiken County, replacing Dr. C. P. Pope, resigned.

Dr. Caroline H. Callison, who for the past four years has served as a County Health Officer in Alabama, in assisting in several Piedmont County Health Departments, with headquarters in Greenwood.

Dr. Edmond J. Bryson, Liberty, has been assigned Health Officer for Pickens County, having previously served as Health Officer for both Oconee and Pickens Counties. Dr. Furman T. Simpson, Westminster, is in charge of Oconee County.

The following physicians have practiced medicine in York County, South Carolina, for the number of years given after their names: Dr. Joseph H. Sayre, Sharon, 62 years; Dr. William A. Hood, Hickory Grove, 56 years; Dr. Charles B. Harrell, Rock Hill, 47 years; Dr. James R. DesPortes, Fort Mill, 45 years; and Dr. James B. Elliott, Fort Mill, 40 years. This record is probably unparelleled in any county of similar population, 58,000, in the United States.

Dr. Alexander Washington Marshall, Charleston, and Miss Sylvia Willis Russell, Haddam, Connecticut, were married recently.

Dr. John Hal Jameson, Easley, and Miss Charlotte Crawford, Savannah, Georgia, were married recently.

Dr. John Emory Holler, Columbia, and Miss Edith Wilhelmina Stuckey, Bishopville, were married recently.

Dr. Robert Alexander Pringle, Charleston, and Miss Barbara Bernice Baldock, Knoxville, Tennessee, were married recently.

TENNESSEE

Tennessee State Medical Association held a special session of the House of Delegates, October 20-21, at the Andrew Jackson Hotel, Nashville.

Dr. D. S. Estridge, associated with Dr. D. N. Williams, Chattanooga, has opened offices at Trenton where he will spend one day each week. He plans later to locate in Trenton and become a permanent resident.

Continued on page 72

Metrazol - *Powerful, Quick Acting Central Stimulant*

COUNCIL ACCEPTED

ORALLY - for respiratory and circulatory support
BY INJECTION - for resuscitation in the emergency

INJECT 1 to 3 cc. Metrazol as a restorative in circulatory and respiratory failure, in barbiturate or morphine poisoning and in asphyxia. PRESCRIBE 1 to 3 tablets, or 15 to 45 minims oral solution, as a sustaining agent in pneumonia and congestive heart failure.

AMPULES - 1 and 3 cc. (each cc. contains 1½ grains.)
TABLETS - 1½ grains.
ORAL SOLUTION - (10% aqueous solution.)

Metrazol, brand of pentamethylentetrazol, Trade Mark reg. U. S. Pat. Off.

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SPENCERS are also Individually Designed for . . .

Fractured Vertebrae
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Osteoporosis
Protruding Disc
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Hernia, if inoperable or when operation is to be delayed
Prenatal-Postpartum Needs
Obesity
Postural Syndrome

And for Patients following . . .

Hysterectomy
Nephropexy
Nephrectomy
Appendectomy
Cholecystectomy
Colostomy
Cesarean Section
Herniotomy
Spinal Surgery
Breast Conditions such as . . .
Ptosed Breasts
Mastitis Prenatal
Nodules Nursing
Prolapsed and Atrophic Breasts
Stasis in Breast Tissues
Following Mastectomy

Sacroiliac or Lumbosacral Disturbances

Relieved and Averted by

Spencer Support

Instability in sacroiliac and lumbosacral areas is effectively checked by a Spencer Support designed to grip pelvis, and provide coordinated abdominal and back support. Thus posture is improved.

Pelvic Band Aids in Inhibiting Movement

A simple pelvic band is incorporated in the support. The band encircles the pelvic girdle *inside* the support and is instantly adjustable from *outside* the support to any degree of snugness required. When the condition subsides, the band may be removed and the remainder of the support worn as a safeguard against recurrence of acute symptoms.

Spencer Supports designed for a man and a woman are pictured *at left*. The small insert shows the band which encircles the pelvic girdle. At center-front of the closed supports can be seen the tapes and slides by which pelvic band may be adjusted without disturbing the support.

Why Spencer Supports Are So Effective

Each Spencer Support is individually designed, cut and made at our New Haven Plant *after* a description of the patient's body and posture has been recorded—and 15 or more measurements have been taken. This assures the doctor that each patient will receive the proper design to aid his treatment; that the support will improve body mechanics and will fit with the precision and comfort necessary. Yet a Spencer costs little or no more than an ordinary support.

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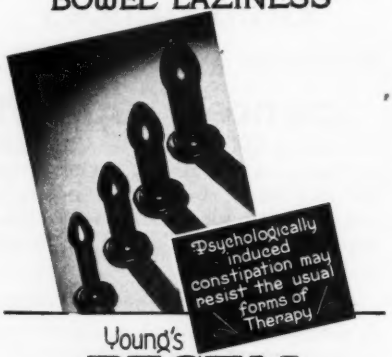
Spencer Supports designed for men are masculine in appearance.

For a dealer in Spencer Supports, look in telephone book under Spencer corsetiere or write direct to us.

SPENCER *INDIVIDUALLY DESIGNED* **SUPPORTS**
Reg. U.S. Pat. Off.
For Abdomen, Back and Breasts

"BOWEL LAZINESS"



Young's
RECTAL DILATORS

Psychologically induced constipation may resist the usual forms of Therapy

Bowel laziness is often the result of unconscious fear—a sort of rectal inferiority induced by prudish notions, pruritus ani or irregular bowel habit. In these cases the rectal muscle is in a state of constant tension and may be compared to a clenched fist. Undue tightness of the anal sphincter is a frequent cause of chronic constipation in children and adults.

This form of bowel laziness can usually be overcome by breaking the impulse of the rectal exit muscle to keep itself locked and Young's Rectal Dilators have been found very effective in restoring sphincter tone. These are four Bakelite dilators graduated in size and introduced in series through the anal canal to the rectum. Their use obviates harsh cathartics and consequent dehydration of the patient.

SOLD ON PRESCRIPTION ONLY

Not advertised to the laity. Set of four graduated sizes, adult, $3.75; children, $4.50. Available for your patients at ethical drug stores or order from your surgical supply house.

Write for brochure today

F. E. YOUNG & COMPANY
450 E. 75th Street Chicago, Ill.

Continued from page 70

Dr. Harold Avent, Memphis, has received a discharge from the Army after serving overseas for a number of months, and will resume his practice in the Physicians and Surgeons Building.

Dr. A. F. Russell, Nashville, has received his discharge from the Army after extensive service in the European theatre of war, and is practicing with Dr. C. S. McMurray in Nashville.

DEATHS

Dr. Samuel D. G. Scruggs, Memphis, aged 95, died recently.

Dr. John Alexander Steward, Chattanooga, aged 47, died recently of cardiac failure.

TEXAS

Texas Ophthalmological and Otolaryngological Society will hold its next meeting at San Antonio, December 7-8, under the presidency of Dr. M. K. McCullough, Dallas.

Texas Society of Pathologists, will hold its next meeting at Dallas, January 27, 1946, under the presidency of Dr. Paul Brindley, Galveston.

A Conference on Pediatrics under the joint auspices of the University of Texas Child Health Program and the Maternal and Child Health Division of the Texas State Board of Health, will be held at the University of Texas Medical Branch, Galveston, November 12-17.

A $40,000 hospital, Clay County Memorial Hospital, is planned to be constructed and dedicated to members of the armed forces of Clay County who lost their lives in World War II as announced by the Henrietta and Clay County Chamber of Commerce. A drive for funds is now being made.

Dr. Warren Andrew, Associate Professor of Histology and Embryology, Southwestern Medical College, Dallas, is doing research at the Laboratory for Histologic Research of the Medical School of the National University of Uruguay, Montevideo, with the collaboration of Dr. Julio M. Sosa, Director of the Laboratory. The work involves a study of microscopic changes in the body with advancing age, and the findings will be published in both Spanish and English. The project is under the auspices of the Uruguayan government and the U. S. Department of State.

Baylor University College of Medicine, Houston, Alumni-Faculty Foundation has been organized to promote and further medical education in Texas by establishing an endowment and foundation in the interest of the welfare of the College of Medicine of Baylor and for aiding and extending work and medical activities in the College of Medicine. Officers are: Dr. Elisha F. Robbins, President; Dr. Herman W. Johnson and Dr. Henry A. Petersen, Vice Presidents; and Dr. Thomas P. Kennerly, Secretary-Treasurer. The creation of a lectureship in memory of the alumni who died during World War II is one of the activities of this Foundation.

Continued on page 74

Classified Advertisements

ESTABLISHED HOSPITAL FOR LEASE — A Sanitarium for nervous, mental, alcoholic and drug cases doing an excellent business available for lease to a reputable physician or medical group. Dr. E. W. Stokes, 923 Cherokee Road, Louisville 4, Ky.

FOR SALE—Maryland home, office attached. General practice in town 1,000, in good agricultural area; churches; school; good highways; can do $10,000 or more first year. Specializing is reason for selling. Write FSJ, care Southern Medical Journal.

WANTED—Physicians for Mental hospital; graduates class A school; experience in psychiatry desirable but not essential; salary and partial maintenance; near two excellent colleges. Address Box 325, Milledgeville, Georgia.

WANTED—Two general practitioners at once for fifty-bed hospital in Alabama. Write MRA, care Southern Medical Journal.

WANTED—Nurses, Dietitians, Laboratory and X-Ray Technicians and Hydrotherapists. Mississippi State Hospital. Whitfield, Mississippi.

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the advanced automatic development of

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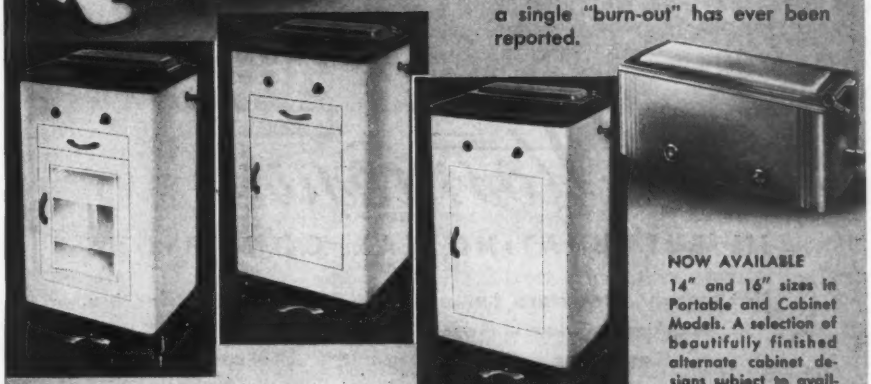

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Continued from page 72

Dr. Charles A. Dwyer, Jr., Houston, for the last three years held a prisoner of the Japanese in Manila's Bilibid Prison, has returned and has been named Psychiatrist for Harris County, succeeding the late Dr. J. B. York.

Dr. L. G. Ballard, Granbury, has been doing postgraduate work in surgery in Kansas City.

Dr. Henry A. Petersen, Houston, is doing post-graduate work in Boston.

Dr. E. G. Causey, El Paso, after three years' service in the Army, has returned to practice in El Paso.

Deaths

Dr. George Delos Beech, Rio Hondu, aged 77, died recently of heart disease.

Dr. Robert C. Bills, Lockhart, aged 80, died recently of cerebral hemorrhage.

Dr. Clarence Frederick Fowler, Galveston, aged 56, died recently of coronary occlusion.

Dr. Buford Allen Russell, Sherman, aged 57, died recently of carcinoma of the liver.

Dr. John Behan York, Houston, aged 73, died recently of uremia.

Dr. Jewel Daughety, Brownwood, aged 58, died recently of carcinoma.

Dr. George Graham Watts, San Antonio, aged 84, died recently of uremia and general sclerosis.

Dr. John Wesley Kennel, San Antonio, aged 74, died recently of paralysis agitans.

VIRGINIA

American Ophthalmological Society will hold its next annual meeting at Hot Springs, The Homestead, November 12-14.

Dr. Elbyrne G. Gill, Roanoke, has been appointed Chairman of the City Board of Health, and Dr. William R. Whitman, Vice-Chairman.

Frederick W. Twymann Fund has been established in the University of Virginia Department of Medicine, Charlottesville,

Continued on page 76

The Makers of *Auralgan* Present

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IN SUPPURATING EAR CONDITIONS

Not merely a mixture but a potent Chemical Combination.

Sulfathiazole-Carbamide in specially dehydrated glycerol "Doho."

Contains the equivalent of about 10% sulfathiazole.

- **EXERTS A POWERFUL SOLVENT ACTION ON PROTEIN MATTER**
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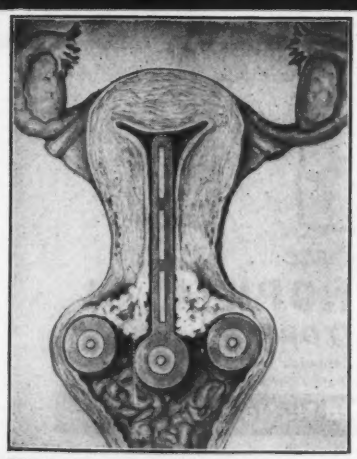

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Continued from page 74

by the sum of $10,000 having been provided in the will of the late Mrs. Sallie B. Twymann as a memorial to her late husband. This fund is to be applied for research in cardiovascular disease under the direction of the Department of Internal Medicine.

Dr. Catherine Bird Hoover, Richmond, and Lieutenant Fordyce Cox Stone, Binghamton, New York, were married recently.

DEATHS

Dr. Thomas Leslie Giles, Toshes, aged 66, died recently of myocarditis.

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FOOD MILL

Conserves mother's time and energy in straining fresh vegetables and fruits. With just a few twists of the wrist, the Foley Food Mill separates fibres and hulls and purees any cooked food fine enough for the smallest baby or for any adult diet — peas, carrots, beets, string beans, spinach, apple sauce, prunes. Made of steel, rust- and acid-resistant. At department and hardware stores.

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Dr. John W. Pierce, Suffolk, aged 65, died recently of heart disease.

WEST VIRGINIA

Central West Virginia County Medical Society has elected Dr. B. L. Page, Buchannon, President; Dr. Ralph M. Fisher, Weston, Vice-President; and Dr. J. M. Cofer, Bergoo, Secretary-Treasurer, re-elected.

Dr. Harold H. Kuhn, Assistant Orthopedist and Instructor in Orthopedics, Duke University School of Medicine, Durham, North Carolina, has located at Charleston with offices in the National Bank of Commerce Building. Dr. Kuhn is a native of Charleston.

Dr. B. J. Moore, Captain, Medical Corps, formerly of Chester, who has been serving overseas, has been honorably discharged from the Army, and has relocated for practice at Morgantown with offices in the First National Bank Building.

Dr. C. Leonard Brown has moved from Nellis to Point Pleasant.

Dr. J. E. Andes, Morgantown, recently of Pulaski, Virginia, has moved to Bozeman, Montana.

Dr. Dewitt T. Bond, Amherstdale, who has been serving with a medical detachment in New Zealand, has been honorably discharged from the Army, and is now in private practice at Danielsville, Georgia.

Dr. Max Koenigsberg, Point Pleasant, formerly Secretary, Mason County Medical Society, has taken up studies in internal medicine at the Graduate School of Medicine, University of Pennsylvania, Philadelphia.

Dr. Walter E. Vest, Huntington, and Dr. Ivan Fawcett, Wheeling, will represent the West Virginia State Medical Association as delegates at the annual meeting of the House of Delegates of the American Medical Association to be held in Chicago, December 3-6. Dr. James L. Wade, Parkersburg, and Dr. W. P. Black, Charleston, are alternate delegates.

Dr. Evelyn Bellaire, formerly of Hinton, has been appointed a member of the staff at Pinecrest Sanitarium, succeeding Dr. William J. Habeeb, who resigned to become Superintendent and Medical Director, Clark County Tuberculosis Sanitarium, Springfield, Ohio. Dr. Bellaire was recently discharged from the service where she was 1st Lieutenant in the Medical Corps at Wollum Lake State Sanatorium, Wollum Lake, Rhode Island.

Dr. Benjamin I. Golden, Elkins, has been appointed Chief Medical Advisor for the West Virginia Department of the American Legion.

Major Joe W. Savage, for seventeen years Executive Secretary, West Virginia State Medical Association, is now with the National Foundation for Infantile Paralysis with headquarters at 120 Broadway, New York City. Mr. Savage who was recently released from active duty with the Army Air Forces, served for over three years with the AAF training command for navigators at various air fields in Texas. He served during World War I as an Army pilot in France for over two years.

Dr. Michael G. Hresan, Major, Medical Corps, Minden, is serving as physician to Arthur Bliss Lane, American Ambassador to Poland, and the members of his staff at Warsaw.

DEATHS

Dr. Flavius Hugh Brown, Summersville, aged 66, died recently of cerebral hemorrhage.

Dr. Eusebius J. Summers, Belva, aged 72, died recently.

"very satisfactory ... in securing prompt and prolonged relief" in bronchial asthma, says Dees (J. Allergy 14:492, 1943) of Aminophyllin rectal suppositories.

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PALATABILITY: The desirable properties of the fish liver oils have been retained without the disagreeable taste and odor.

HOMOGENIZATION: This assures a uniform and stable product that permits of easy miscibility with milk, special formulae, fruit or vegetable juices, or with water.

HIGH VITAMIN POTENCY: 5,000 U.S.P. units of vitamin A and 500 U.S.P. units of Vitamin D3 supply the daily minimum requirements (FDA) in one teaspoonful.

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EASY ADMINISTRATION is possible because of unusual potency of small dose.

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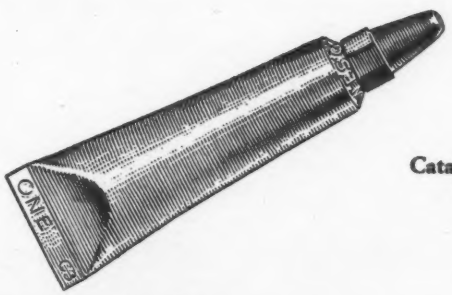

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Rachitic changes were present as late as the fourteenth year, and the incidence was higher among children dying from acute disease than in those dying of chronic disease.

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*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 1943.

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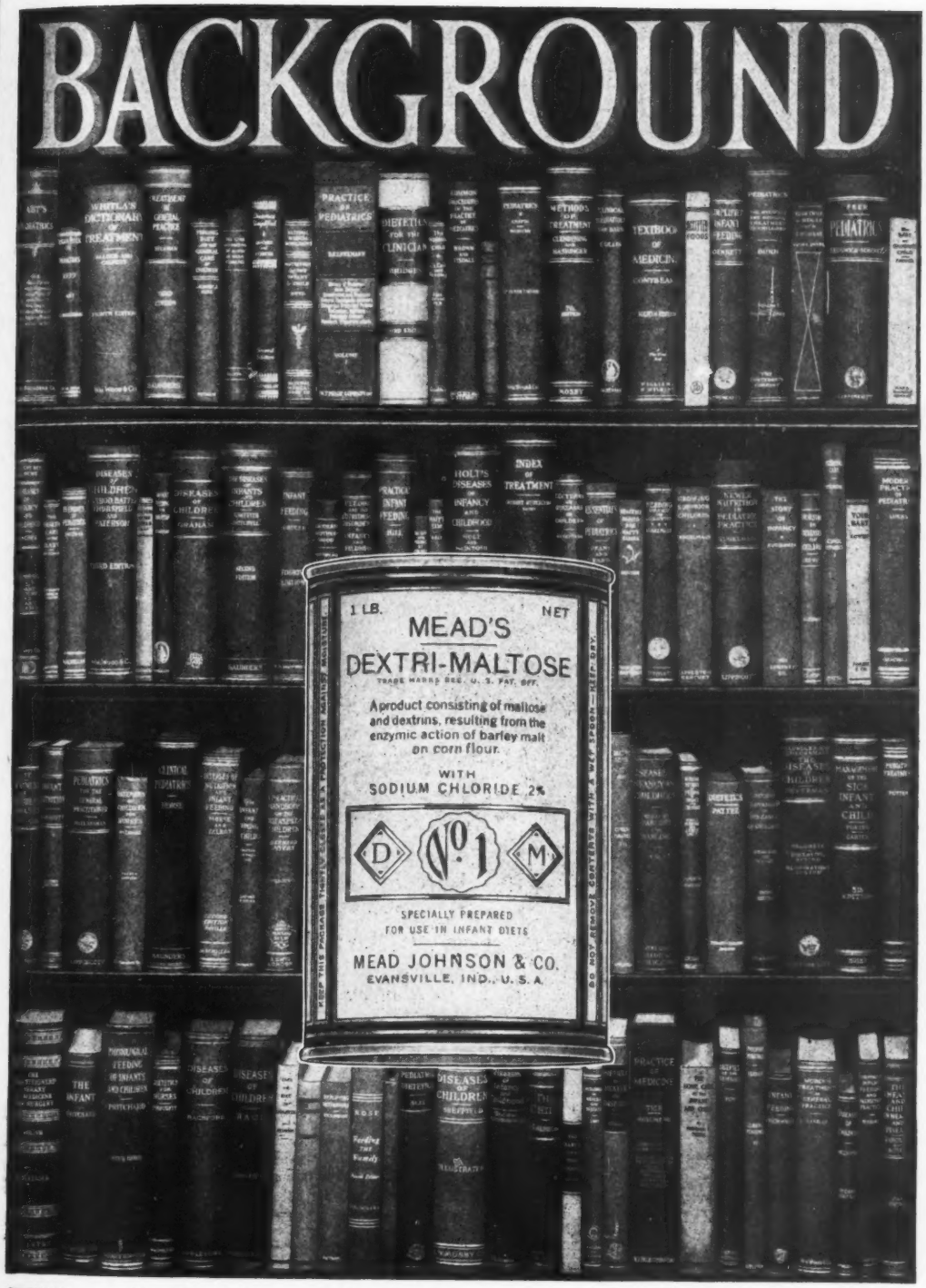

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